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TREND OF PEDIATRIC EDUCATION AND PRACTICE

PRESIDENT'S ADDRESS

BORDEN S. VEEDER, M.D.
ST. LOUIS

In the twenty-five years that have passed since 1910 when I attended my first meeting of this society, the growth and development of pediatrics have been among the remarkable phenomena of American medicine. This holds true whether one considers the part pediatrics has played in the total growth of medical sciences, scientific investigation and the material growth of clinics and hospitals, the position of pediatrics in the structure of medical education, the place it occupies in medical practice or the part it has played in the changed social relationships of medicine, as in every phase the development has been striking. It has been a rare privilege to watch this change taking place and to be associated with the members of the American Pediatric Society, who have furnished the leadership in this development.

This development may be looked on as reflecting the rapid changes that have taken place in the environment and the organization of the social structure in the United States during this time. Dr. Ruhräh, in discussing the progress of pediatrics through the ages, held that it was but the product of environment in any age. Although the historical perspective is lacking, I believe this premise holds true when one considers what has happened to the environment and social structure in this country during the past twenty-five years. In a broad way the revolution that has taken place has been the result of two trends, one mechanistic and the other social, and these forces have in the last analysis brought about the changes in pediatrics. Unfortunately, the two forces have not always led to the same goal, and in a way similar to that in which society finds itself faced with certain perplexing problems of fundamental significance for its future direction, pediatrics at the present moment is faced with certain problems or dilemmas. I wish today to discuss briefly a few of the trends in pediatrics in the last twenty-five years. There are many trends that merit discussion, but as I still find myself sufficiently naive and childlike to believe that

Read at the meeting of the American Pediatric Society at Cleveland, May 2, 1935.

the most important function of the physician is to practice medicine and of the medical school to train and educate the physician, I have chosen certain of the social and educational trends of pediatrics which have led to the present-day problems of education and practice.

The social trend has become the urgent medical problem of today, as it implies widespread changes in the practice of medicine. It is far from my purpose to speak of the broad aspects of this problem, for in this particular discussion social influences are of interest only as they have affected pediatric education and practice. The rise of pediatrics in recent years has gone hand in hand with the interest of society in the welfare of the child. I am quite sure that pediatrics would never have undergone such rapid development had it not been for this outside influence demanding a vague something from medicine which the physician of twenty-five years ago was not prepared to give. I am further of the opinion that much of the material means which has permitted the physical development of the present departments of pediatrics has been due directly to this social trend. While the movement for child welfare has involved the usual amount of wasted effort, misdirected energy and the like that goes with any social movement, it has, however, been a definite factor in the changed conception of the scope of pediatrics. The centering of interest on the child rather than on disease in childhood is largely responsible for the development of pediatrics as a distinct field in the formulation of the medical curriculum as well as in practice, and so the importance of the social influence must be acknowledged.

One of the direct influences of the social trend on practice has been the child welfare clinic. In the report of the Third White House Conference it was estimated that 10 per cent of the child population of this country has at some time been enrolled at a welfare clinic. In some urban areas the proportion rises as high as 30 per cent. Social workers, and even at times physicians, are likely to attribute the reduction in the mortality and the morbidity rate among infants and children to the clinic, ignoring such important hygienic factors as improvement in the milk and water supply and better housing, as well as such important biologic factors as natural immunization. That there is a place for the welfare clinic is obvious, and I know of no other mechanism that will take its place for certain social and economic groups. But one is likely to forget that it is nothing but a mechanism for applying pediatric knowledge, a method rather than a goal. I have elsewhere stated my point of view that it is a rather inferior technical method of applying pediatric knowledge to the supervision of the developing infant and child. The unsound and illogical separation of the child when well from the child when sick, the lack of continuity in the supervision as a result of the continually changing character of the personnel of the clinic and of the administrative methods at different

age periods together with the lack of specific personal knowledge of the child's background and environment, which cannot be replaced by a social worker's report, are among the factors which to my mind make public health or mass methods of supervision decidedly inferior from a technical standpoint, and hence they should be developed and emphasized as a substitute only when nothing better is available medically and economically. I am sure that the argument in vogue from ten to fifteen years ago that physicians as a rule were not prepared to give adequate supervision to the developing child is rapidly losing its truth. The future danger, as I see it, lies in sociologists and welfare workers, who as a group have a very limited background and heritage of experience as compared with the medical profession, attempting through social legislation to extend the clinic or public health method, which is at best inferior to continuous individual supervision throughout infancy and childhood by the trained and qualified physician. It is very unfortunate, to my mind, that the opposition to the child welfare clinic on the part of the medical profession has been based on such considerations as state medicine, undeserved charity and the like rather than on its being an inferior technical method of child care and supervision. Opposition to its extension should be based on the fact that the medical profession has something better to offer.

In the few years prior to 1910 what might be termed the revolution in medical education in the United States began to get under way. Studies by foundations and by the American Medical Association had focused attention on the deplorable state of medical education. What has been accomplished is a familiar story. The development of teaching equipment in the way of hospitals, laboratories and institutions for research paralleled definitely the mechanization of American life during the last quarter of a century. But there has been an overemphasis on physical equipment, which has produced some of the same troubles that came with the overdevelopment of industry. False ideas of competition led to the development of some institutions to a point far beyond practical needs and even to a degree at which physical development became a burden detrimental to the purpose for which they were established. All too many vacant or partially empty educational palaces are found today as the result of mistaking physical size and grandeur for a necessary attribute of quality. It is the same spirit of "size" which has dominated so many other phases of American life.

As a part of this revolution the number of medical schools in America has fallen from 160 in 1904 to less than 80 at the present time. The number of graduates each year decreased from 5,747 in 1904 to about 3,000 in the early years of the 1920's. Every one is seemingly in agreement that not more than the latter number can be absorbed yearly into the profession of medicine. But the 77 remaining schools

graduated 5,038 physicians in 1934—far more than can be fitted into the field of medical practice. The present schools are unwilling to cut their enrolment, as the tuition fees are necessary to maintain their budgets. It is a curious whirl. Medical schools were built up in an expensive way until the overhead cost became enormous. This growth was based on the ideas that such development was necessary for the education of the physician. Many institutions became in reality institutions of medical research, and the education of the student came to be only one of a number of functions. In order to maintain this elaborate set-up more and more students were enrolled in the last decade for the sake of tuition fees, until now the number is again as high as when the commercial schools ruled the field. More medical students than can be absorbed into the field of medical practice are being encouraged by the medical schools to enter on the costly study of medicine. It is a rather stupid situation, which is not only unfair to the student but potent with danger to medicine as a whole. As recently happened in industry, the medical schools have developed their institutions to a point of overproduction with a blind disregard for the disposal of their product. Unless remedial measures are instituted one can look forward to a chaotic situation similar to that seen in industry in the last five years.

The status of pediatrics in 1910 is well described by the following reference by Dr. Edsall in his address to a conversation with "one of the ablest educators in this country": He "told me most forcibly that an extended inspection of medical schools had convinced him that, considering its importance, pediatrics is more inadequately provided for in most medical schools than any other important subject. . . . The conditions surrounding it are, in most places, shameful." No one familiar with the situation at that time will question the truth of this statement. When one looks on the number of excellent pediatric clinics in America today it is difficult to realize that prior to 1910 adequate undergraduate training in pediatrics did not exist and that it was necessary for any one desiring graduate work and training to study abroad. Today the vast majority of medical schools have adequate clinical material and facilities for teaching pediatrics. At least 12 clinics have been developed to the point where splendid facilities in the way of leadership, laboratories, equipment and funds for research are available. Twenty-five years ago pediatrics was a minor, unimportant subject in medical education. The situation has completely changed since that time.

No knowledge of the time allotted in the curriculum to the teaching of pediatrics in 1910 is available. The first survey of this nature was made in 1929-1930, only five years ago, by a committee of the Third White House Conference, which found that 67.5 per cent of the schools

allotted less than 200 curriculum hours to pediatrics. This was the number of hours arrived at in the study as necessary for adequate teaching of the subject. In at least 35 per cent of the schools the time allotted was beyond question inadequate. In a survey made the past year it was found that in the curriculum for 1934-1935 50 per cent of the schools allotted 200 or more hours and that in only 16 per cent could the number of hours assigned be considered inadequate. It is exceedingly difficult to make comparisons on the basis of the number of hours, as many schools offer elective hours in addition to those required and the utilization of hours is varied from a pedagogic standpoint. There is an increasing tendency to utilize the method of clinical clerks in teaching pediatrics, and the number of hours on this basis is difficult or impossible to calculate, particularly in many instances in which the student is assigned to the pediatric wards for from "a week" to " a month," as the case may be. Hence, statistics are important simply as indicating trends. The following tabulation of data obtained

Summary of Required Hours in Forty-Two Schools

Year	Under 100	100 to 150	150 to 175	175 to 200	200 to 225	225 to 300	Over 300
1929-1930	4	12	7	6	6	5	2
1934-1935	0	7	9	5	7	6	8

from 42 schools shows not only the decrease that has taken place in the number of schools in which the allotment of hours falls in the lower brackets but the increase in the last few years in the number of assigned or required hours over the minimum standard mentioned in the report of the Committee of the White House Conference. Eighteen of the schools offer in addition elective hours in pediatrics.

All this is important only as it shows the tendency to acknowledge the importance of pediatrics in the formulation of the medical school curriculum which has taken place in the last twenty-five years. The result of this change is that the graduate of recent years has entered on his career as a physician with a good working knowledge of pediatrics. It is no longer a field of mystery and fear as it was to the graduate of twenty-five years ago. The recent graduate who has gone into general practice is able, I believe, to give fairly adequate service to the vast majority of infants and children who come under his care. This is what has been striven for—the provision of better medical care for the children of America—and this purpose is rapidly being accomplished by the increased attention to, and improved teaching of, pediatrics in

the medical school. If the vast majority of illnesses and the nutrition and development of the infant and child cannot within a few years be adequately looked after by the general practitioner there is something wrong in the present pediatric pedagogy. I emphasize this trend in general undergraduate instruction, as it has a most important bearing on the question of specialization.

One of the striking phenomena of American medicine in recent years has been the trend toward specialization in practice. While this can perhaps be looked on as a mechanistic tendency in that it has resulted from the growth of medicine as a science, as well as having a commercial aspect, so far as pediatrics is concerned there is also a social reason in that during the last fifteen years consciousness of the child has been an outstanding trend of social thought. In 1934 32.6 per cent, or nearly one third, of the physicians in active practice in the United States were listed as limiting their practice to, or declaring particular interest in, a specialty. One in approximately every 12 of this number was in the field of pediatrics. Until the last two years little has been done to control or regulate the special fields, and the trained and educated physician has practiced side by side with the untrained, self-styled specialist.

Pediatrics developed fairly late as a special field of practice. It is clear from his writings that Dr. Jacobi, while urging special training in pediatrics in the medical school, was not an advocate of pediatrics as a special field of practice. Dr. Morse stated that in 1890 there were only 49 members of this society, which included all the pediatricians in the country, and that not a single man limited his practice to children. As late as 1910 the roster of the society contained the names of many who would have been the last to designate themselves pediatricians, such as Dr. Edsall, the president of that year.

In order to show the rapid growth and development of specialization in pediatrics in the last twenty-five years, I compiled the statistics from the medical directory of 1914—the first year that designations for specialists were used—and compared them with those for 1921 and 1934.

This trend can be more graphically expressed by stating that in 1914 1 physician in every 1,031 limited his practice to pediatrics; in 1921, 1 in every 218, and in 1934, 1 in every 90. The proportion of all physicians who were interested in pediatrics changed in the last twenty years from 1 in 162 in 1914 to 1 in 41 in 1934.

In no other special field has there been such a rapid increase of practitioners, nor has specialization been so popular. Dr. Weiskotten, in studying in 1928 the graduates of the classes of 1915 and 1920, found that while the percentage of graduates limiting themselves to surgery,

internal medicine and diseases of the eye, ear, nose and throat had decreased, the percentage of those specializing in pediatrics had increased from 5.8 for the class of 1915 to 11.1 for the class of 1920, or an increase of nearly 100 per cent in the five year interval. The percentage as a whole, moreover, for graduates who had limited their practice to one field had fallen from 42.5 for the class of 1915 to 36.1 for that of 1920. The development of pediatrics as a special field has thus been at a rate far beyond the increase of specialization as a whole.

Mechanization, such as the development of children's hospitals and of pediatrics as a distinct department in the medical school, does not alone account for this growth. It has most certainly been due in part to the social trend of recent years, that is, to the increased sense of responsibility for the child on the part of society. Public health propaganda, school activities, the newspaper columns, radio broadcasts and the like have educated parents to demand something special for

Statistical Summary Concerning Specialization in Pediatrics for the Last Twenty-five Years

Year	Number with Practice Limited to Pediatrics	Number Giving Special Attention to Pediatrics	Total Number
1914	138	741	879
1921	664	1,798	2,462
1934	1,734	2,155	3,889

their children in the way of medical service, and the specialist in pediatrics as he now in large part exists has prepared to supply this demand. It has been a demand that has gone far beyond the question of disease in childhood. I think no one will question the truth of the statement that until recent years the average graduate from a medical school did not possess sufficient knowledge of pediatrics to give adequate supervision to the child—hence the rapid increase in the number of pediatricians in medical practice. But the specialist in pediatrics is quite a different person from the specialist in other medical fields. I am sure that physicians will agree with me without argument that the pediatrician in practice is a general practitioner of medicine who limits his work to patients of a certain age period. All but a negligibly small percentage of pediatricians are in practice, and the term pediatrician must be defined on that basis.

It is of importance in this connection to consider the present rate at which specialists in pediatrics are being turned out—not only the rate but the prospects which are dangled in the faces of young medical

men. A committee of the American Academy of Pediatrics has been compiling the opportunities for twelve month positions as interns, assistant residents and residents in pediatric services in hospitals approved by the Committee on Medical Education of the American Medical Association. Approximately 300 positions are open yearly. Requirements of the American Board of Pediatrics for certification, in accordance with the regulations of the American Medical Association, call for, as a part of the requirement, two years of work in a pediatric clinic. Thus, 150 well trained men could be added yearly to the group of men in practice who are now specializing. In order to find what has happened to the men who were trained in pediatric clinics in recent years I reviewed the records of the house officers of the St. Louis Children's Hospital for the period from 1915 to 1930. A little over 80 per cent of the men are now actively engaged in the practice of pediatrics. If this rate is applied generally, an increase of 120 qualified trained men can be looked for yearly, which will bring the total number to at least 3,000 by 1944 if conditions continue as at present. To these a number of unqualified, inadequately trained specialists will undoubtedly be added, although I am sure the number will be much less than in the past. The question faces one: Can these men be absorbed as pediatric specialists? Frankly, I doubt it. I question not only the present-day opportunity but the need for so large a number.

This raises an interesting side question as to whether the pediatric services in the hospitals will continue to attract men on the basis of conditions existing at present. When the young graduate finds that pediatrics as a specialty fails to offer him a satisfactory professional outlet and monetary return he will hesitate before entering on the long, expensive training which specialization demands. I would not be surprised to find that in a few years many of the children's hospitals will have to use their intern services as a part of general intern training and will be able to fill only the residentships with men who intend to specialize.

One is thus faced with a situation brought about by these various trends in pediatrics, as the specialty has developed in the past twenty-five years, which I believe merits serious thought on the part of those who are leaders and hence are responsible for educational trends. It is for this reason I have chosen to discuss the matter before this society.

A social demand has created a large group of pediatric specialists to meet a need that could not be supplied by the average practitioner of medicine of a few years ago. This group has developed at a tremendous rate, and the pediatric clinics are filled with promising young men who expect to enter this field and find a successful professional life. Coincident with this, public health methods for the medical supervision

of the child have been developed as a response to the same demand, which at the present time offer medical supervision for a large part of the child population. During this period a marked development and change in the teaching of pediatrics have taken place in the medical schools. The average recent graduate should be able to care for and supervise the development of the infant and child; if not, the fault is in the present pedagogic system.

Three mechanisms have thus been developed to meet the same demand. A point has been reached, I believe, at which these mechanisms more than meet the demand, and a definite change in trends must necessarily follow.

Macaulay stated: "Knowledge of past events is invaluable only as it leads us to form just calculations with respect to the future." It is rather hazardous to express "just calculations" at present in view of the important social trends of society and particularly when socialization of medicine looms so large on the horizon. With full realization that the "just calculations" of today may therefore seem amusing to a chance reader a few years hence, I believe that it is nevertheless important to attempt to see the way out.

First of all, I believe that in a few years the general practitioner will take over a large part of the work that is being done by the specialist in pediatrics as he now exists. This change appears to me the logical result of the changed place of pediatrics in the curriculum of the medical school. It will be all the more a factor in view of the excessive number of physicians being turned out of the medical schools—a situation that should be corrected.

Public health methods of child care and supervision will increase because of economic conditions and general social trends. Whether such a mechanism is increased to a point at which the majority of children will be thus looked after depends on the ability of the medical profession to point out that it is an inherently inferior technical method of utilizing pediatric knowledge rather than on opposition to it on the grounds of state medicine.

The pediatrician, as he exists in practice today and as he has developed so rapidly in the last few years, will find the need and opportunity for him rapidly diminishing as the general practitioner becomes able to take over his work and as public health methods are continued in the form in which they now exist, or even as they perhaps increase. The trend toward specialization in pediatrics will decrease, and further the type of work of the pediatrician will, to a certain extent at least, change. He must eventually be a much better and more thoroughly trained man than he has been in the past. Specialization will be much better regulated and controlled than in the past. The

boards on qualifications for specialties which are attempting to place specialization on an educational basis are but the first step in this direction.

It is not that a changing situation is any particular reason for worry or alarm, as in the long run conditions automatically find a solution. It is necessary, however, to realize that conditions are changing and that it is for these who are leaders to meet changed conditions and trends. Above all, young medical men must not be encouraged to enter blindly into a field of practice which, as it at present exists, is rapidly becoming limited in its opportunities and future.

ANTIRACHITIC EFFECTS OF RADIATION FROM DIFFERENT SOURCES

A COMPARATIVE STUDY

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This investigation was undertaken to determine the comparative biologic value of radiations from different kinds of lamps. Since the antirachitic effect of radiation has been more thoroughly studied and more accurately standardized, it was decided to use the rachitic rat as an indicator. Since the total reaction obtained varies somewhat with different rachitogenic diets, it seemed desirable to make simultaneous studies on groups of rats fed different diets. Accordingly, the Steenbock 2965 and the McCollum 3143 rachitogenic diets were selected as the ones probably most widely used.

Six series of experiments are reported. In series 1 only the Steenbock diet was used; in series 2 only the McCollum diet. In all other series duplicate tests were made with each diet.

In some of the experiments the line test was employed as a check on the roentgenographic readings, but it was found that there was generally such close agreement that the line test was not used in later experiments. In every series, roentgenograms were made at the beginning of the experimental procedures, in some cases of the entire group, but usually of only a few animals in each group. The animal was lightly anesthetized with ether and placed in the desired position, and the exposure was made, the entire procedure requiring about two minutes. Careful observation and frequent weighings failed to show that any deleterious effect was produced on the animal. Terminal roentgenograms were always made after death.

Ten different lamps were used in the course of the investigation, the selection being based mainly on availability. For seven of the lamps the energy incidence and distribution were determined at the distances

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From the Department of Physiology, College of Medicine, University of Illinois.

The expenses of this investigation were borne in part by grants from the American Association for the Advancement of Science, the American Medical Association, the University of Illinois Graduate School Research Fund and the Phi Rho Sigma medical fraternity.

employed in the experiments. Groups of from three to four albino rats were caged together. In all but series 6 the treatment was applied within three days of the time the animals were placed on the experimental diet. The Hendryx type of nutrition cages were used. These were kept in rooms with only a northern exposure, and, in addition, the rats in series 6 were confined in a room which was practically completely darkened. Every precaution was taken in controlling extraneous conditons.

THE PROTECTIVE VALUE OF VARIOUS LAMPS

Series 1 (Table 1).—In this series a comparison of the carbon arc projector lamp and the small air-cooled quartz mercury vapor arc lamp was made. Several variations of these experiments were introduced, but the results are not included

TABLE 1 (Series 1).—*Data for Male Rats on the Steenbock Diet Treated for Seven Weeks During the Spring with a Carbon Arc Projector Lamp with Blue Flame Carbons* at 10 Inches and with a Small Air-Cooled Quartz Mercury Vapor Arc Lamp at 6 Inches*

Group	No. of Rats	Average Initial Weight, Gm.	Average Maximum or Terminal Weight, Gm.	Growth Ratio†	Exposure Time, Minutes: Minimum per Day	Exposure Time, Minutes: Maximum per Day	Exposure Time, Minutes: Total	Lamp	Rickets‡
2 (Controls)	5	44	58	0.205	..	..	...	.....	Very severe
3	4	45	69	0.436	15	60	975	Carbon arc	None
4	4	43	69	0.467	10	60	900	Air-cooled mercury vapor	None

* Manufactured by the National Carbon Company, Cleveland.

† The growth ratio equals $\frac{\text{maximum or terminal weight minus initial weight}}{\text{initial weight}}$.

‡ The diagnosis of rickets was made by means of roentgenograms and line tests.

in table 1 as they add nothing to the information obtainable from the three groups that are reported on in the table.

The degree of protection against rickets was practically identical with the two lamps and there were no significant differences in the rate of growth in the rats, although in neither case was the rate comparable to that of rats fed normal diets. In group 3 there was considerable fluctuation in weight.

Series 2 (Table 2).—When this experiment was undertaken, the lamps that had been used in series 1 were not available but three other lamps were secured: a water-cooled quartz mercury vapor arc lamp and two models of the quartz mercury bulb lamp. For two of these and for all subsequent experiments the energy incidence in calories per square centimeter per minute was determined for the distances at which the exposures were made. Only the McCollum rachitogenic diet was used in this series.

The water-cooled quartz mercury vapor arc lamp and the first model of the mercury bulb lamp offered complete protection against rickets with five minute exposures, although the former was practically as effective with one minute exposures. The second model of the mercury bulb lamp, however, did not give complete protection with three hour exposures. The first model with thirty minute exposures inhibited growth during the first week, but thereafter the curve was

practically parallel with the curves for one and for five minutes. Of all the experiments in this series the first model of the quartz mercury bulb lamp at one minute produced the best growth but the least protection, and the water-cooled quartz mercury vapor lamp gave the best protection but produced a relatively slow rate of growth. The third lamp (second model of the quartz mercury bulb lamp) was unquestionably the least efficient.

Series 3 (Table 3).—Since some observations of a general nature made in series 1 and 2 suggested a difference in the responses obtained that might be related to the diets, it was decided to study another series of rats, using two diets. Since

TABLE 2 (Series 2).—*Male Rats on the McCollum Diet Treated for Seven Weeks During May and June with a Water-Cooled Quartz Mercury Vapor Arc Lamp at 4 Inches and Two Quartz Mercury Bulb Lamps at 15 and at 5 Inches, Respectively*

Group	No. of Rats	Average Initial Weight, Gm.	Average Maximum or Terminal Weight, Gm.	Growth Ratio	Exposure Time, Minutes: Daily	Exposure Time, Minutes: Total	Calories per Square Centimeter per Minute	Lamp	Rickets
11 (Controls)	4	39.0	181	3.500	..	.....	.....	.....	None
1 (Controls)	4	39.5	64	0.525	..	.....	.....	.....	Very severe
2	4	41.0	77	0.870	1	49	.....	Water-cooled mercury vapor	Complete protection
3	4	40.5	90	1.250	1	49	20.1×10^{-4}	Mercury bulb	Severe, less than in group 1
4	4	40.5	69	0.720	2	98	18×10^{-4}	Mercury bulb, second model	Very severe
5	3	41.0	82	1.000	4	196	.....	Water-cooled mercury vapor	Complete protection
6	3	40.0	87	1.150	5	245	20.1×10^{-4}	Mercury bulb	Complete protection
7	3	41.0	83	1.020	30	1,470	18×14^{-4}	Mercury bulb, second model	Severe
8	3	42.0	85	1.070	30	1,470	.....	Water-cooled mercury vapor	Complete protection
9	3	41.0	85	1.070	30	1,470	20.1×10^{-4}	Mercury bulb	Complete protection
10*	3	39.0	82	1.050	180	8,820	18×10^{-4}	Mercury bulb, second model	Mild

* The three rats in group 10 grew slowly, especially during the first week, and showed an irregular growth curve.

the water-cooled quartz mercury vapor arc lamp gave complete protection with one minute daily exposures it was discarded in this series. Since the quartz mercury bulb lamp (first model) offered little protection at one minute and complete protection at five minutes, it seemed important to determine, if possible, a more definite threshold of protection. Also, it seemed of some importance to determine whether or not there was any difference in response to the mercury bulb lamp (second model) in relation to the diet. Since the air-cooled quartz mercury vapor arc lamp is in common use, it seemed advisable to substitute a lamp of this type (second model) for the water-cooled lamp.

The daily periods of exposure for each lamp were two, five and thirty minutes. The shorter periods were selected in an effort to localize the threshold. The longer period was used to determine whether or not it would induce a more rapid rate of growth.

TABLE 3 (Series 3).—*Duplicate Groups of Rats on the McCollum and Steenbock Diets Treated for Seven Weeks During November and December with a Quartz Mercury Bulb Lamp at 15 Inches, a Second Model at 5 Inches and an Air-Cooled Quartz Mercury Vapor Arc Lamp at 11 Inches*

Group	No. of Rats	Average Initial Weight, Gm.	Average Maximum or Terminal Weight, Gm.	Growth Ratio	Exposure Time, Minutes		Calories per Square Centimeter per Minute	Lamp	Diet	Rickets
					Daily	Total				
1 (Controls)	3	32	196	5.44	..	.....	.....	.....	Wistar	None
3 (Controls)	3	33	81	1.45	..	.....	....	.....	McCollum	Severe
4 (Controls)	3	33	67	1.03	..	.....	.....	.....	Steenbock	Severe
5	3	33	73	1.21	2	98	20.1×10^{-4}	Mercury bulb	McCollum	Moderate
6	3	33	69	1.09	2	98	20.1×10^{-4}	Mercury bulb	Steenbock	Severe
7	3	34	71	1.09	5	245	20.1×10^{-4}	Mercury bulb	McCollum	Slight
8	3	33	63	0.91	5	245	20.1×10^{-4}	Mercury bulb	Steenbock	Severe
9	3	32	94	1.96	30	1,470	20.1×10^{-4}	Mercury bulb	McCollum	Complete protection
10	3	32	70	1.18	30	1,470	20.1×10^{-4}	Mercury bulb	Steenbock	Slight
11	3	34	95	1.80	2	98	35.8×10^{-4}	Air-cooled mercury vapor, second model	McCollum	Slight
12	3	32	62	0.82	2	98	35.8×10^{-4}	Air-cooled mercury vapor, second model	Steenbock	Slight
13	3	34	83	1.44	5	245	35.8×10^{-4}	Air-cooled mercury vapor, second model	McCollum	Complete protection
14	3	33	60	0.82	5	245	38.5×10^{-4}	Air-cooled mercury vapor, second model	Steenbock	Very slight
15	3	33	84	1.24	30	1,470	35.8×10^{-4}	Air-cooled mercury vapor, second model	McCollum	Complete protection
16	3	33	60	0.82	30	1,470	35.8×10^{-4}	Air-cooled mercury vapor, second model	Steenbock	Complete protection
17	2	33	102	2.09	5	245	18.0×10^{-4}	Mercury bulb, second model	McCollum	Severe
18	2	33	66	1.00	5	245	18.0×10^{-4}	Mercury bulb, second model	Steenbock	Severe
19	2	34	93	1.44	30	1,470	18.0×10^{-4}	Mercury bulb, second model	McCollum	Moderate
20	2	33	67	1.03	30	1,470	18.0×10^{-4}	Mercury bulb, second model	Steenbock	Severe

Throughout this entire series it is apparent that the rats on the Steenbock diet responded less favorably, regardless of the treatment, than did those on the McCollum diet, both in regard to the rate of growth and in regard to the degree of rickets. Also, the results make it clear that the air-cooled quartz mercury vapor arc lamp (second model) gave the best results, and the mercury bulb lamp (first model), the next, so far as the antirachitic effects were concerned, but there is much less conclusive evidence as to the relation of the source of light to the rate of growth. The best curves for growth were produced with the air-cooled mercury vapor arc lamp and the mercury bulb lamp (second model), with a slight margin in favor of the latter, especially when all of the terminal weights were averaged together in all of the groups treated by the same lamp, regardless of time.

The energy incidence for the mercury bulb lamp (first model) at the distance used in this experiment was 20.1×10^{-4} calories per minute; for the air-cooled mercury vapor arc lamp (second model), 35.8×10^{-4}, and for the second model of the mercury bulb lamp, $18 \times {}^{10-4}$. These figures are in direct relation to the antirachitic effects.

The experiments in series 3 were carried out in November and December, and those in series 2, in late spring (May and June). To our surprise even the thirty minute exposure to the mercury bulb lamp (first model) in series 3 did not offer complete protection, whereas five minute exposures had been sufficient in series 2. The subjects of the latter series were born in late winter or early spring; those in series 3 were born in late autumn.

Series 4 (*Table 4*).—It was next decided to carry out another experiment on rats born in midwinter. A new model (third) of the quartz mercury bulb lamp was secured which gave a higher energy incidence. Also, another model (third) of the air-cooled quartz mercury vapor arc lamp and a mercury vapor glow lamp were used. The experiments were begun on March 17.

As in the other series, the groups of rats on the Steenbock diet in series 4 grew less rapidly than those on the McCollum diet with the exception of the two rachitic control groups. The best rates of growth were obtained in groups 9 and 10, in which the rats were irradiated with the mercury bulb lamp (third model) for thirty minutes; and in group 13, in which they were irradiated with the mercury vapor glow lamp for thirty minutes. The rats in groups 11 and 12, exposed to the air-cooled quartz mercury vapor lamp (third model) for thirty minutes, grew little better than the rachitic controls. Curiously, the rate of growth for group 3 was much better than in any of the similar groups in series 2 (groups 3, 6, and 9) or in series 3 (groups 5, 6, 7 and 8), even better than in the animals given thirty minute exposures in series 3 (groups 9 and 10). However, the degree of rickets in group 3 was much more severe than in any of the groups of rats that had been treated, while there appeared to be good protection in the corresponding group of rats on the Steenbock diet (group 4). The degree of protection against rickets was comparable in the two diet groups up to group 11. From there on the response was definitely in favor of the groups of rats on the McCollum diet. With the longer exposures, the rate of growth was retarded slightly in all the groups on the Steenbock diet and also markedly in the group on the McCollum diet exposed to the air-cooled quartz mercury vapor arc lamp (third model, group 11). The behavior of the rats in groups 3 and 4 cannot be accounted for at present; possibly the extremely slow rate of growth in group 4 may account for the milder degree of rickets in this group as compared with that in group 3; up to the end of seven weeks the rate was below that of any other group. Thus, in this series the best rate of growth was produced by the

TABLE 4. (Series 4).—*Duplicate Groups of Rats on the McCollum and Steenbock Diets Treated for Seven Weeks, Beginning March 17, with a Quartz Mercury Bulb Lamp at 15 Inches, an Air-Cooled Quartz Mercury Vapor Arc Lamp at 21 Inches and a Mercury Vapor Glow Lamp at 10 Inches*

Group	No. of Rats	Average Initial Weight, Gm.	Average Maximum or Terminal Weight, Gm.	Growth Ratio	Exposure Time, Minutes		Calories per Square Centimeter per Minute	Lamp	Diet	Rickets
					Daily	Total				
18 (Controls)	3	43	203	3.72	..	.....	.....	.....	Wistar	None
1 (Controls)	4	35	78	1.23	..	.....	.....	.....	McCollum	Very severe
2 (Controls)	4	44	87	0.98	..	.....	.....	.....	Steenbock	Very severe
3	3	40	89	1.22	5	245	67×10^{-4}	Mercury bulb, third model	McCollum	Moderate
4	3	44	71	0.61	5	245	67×10^{-4}	Mercury bulb, third model	Steenbock	Mild
5	3	41	98	1.39	5	245	155×10^{-4}	Air-cooled mercury vapor arc, third model	McCollum	Mild
6	3	44	90	1.04	5	245	155×10^{-4}	Air-cooled mercury vapor arc, third model	Steenbock	Slight
7	3	43	100	1.32	5	245	117×10^{-4}	Mercury vapor glow	McCollum	Slight
8	3	41	88	1.19	5	245	117×10^{-4}	Mercury vapor glow	Steenbock	Slight
9	3	40	105	1.63	30	1,470	67×10^{-4}	Mercury bulb, third model	McCollum	Nearly complete protection
10	3	41	97	1.37	30	1,470	67×10^{-4}	Mercury bulb, third model	Steenbock	Slight
11	3	43	87	1.05	30	1,470	155×10^{-4}	Air-cooled mercury vapor arc, third model	McCollum	Complete protection
12	3	43	87	1.02	30	1,470	155×10^{-4}	Air-cooled mercury vapor arc, third model	Steenbock	Complete protection
13	3	40	103	1.57	30	1,470	117×10^{-4}	Mercury vapor glow	McCollum	Complete protection
14	3	39	83	1.12	30	1,470	117×10^{-4}	Mercury vapor glow	Steenbock	Complete protection

mercury bulb lamp (third model) at thirty minutes, with a decided margin in favor of the mercury vapor glow lamp for antirachitic protection. However, when all of the ratios are averaged for each lamp, there is so little difference that it is questionable how much significance may be assigned to this relationship.

The energy incidence for the various lamps used in this series was as follows: for the mercury bulb lamp (third model), 67×10^{-4} calories per minute; for the mercury vapor glow lamp (first model), 117×10^{-4}, and for the air-cooled mercury vapor arc lamp (third model), 155×10^{-4}. Everything considered, the mercury vapor glow lamp gave the best protection when the two diet groups are considered together. It may be that the higher energy incidence of the air-cooled mercury vapor lamp in some way acted unfavorably, possibly by inactivating or decomposing the vitamin.

Even at thirty minutes the mercury bulb lamp (third model) did not afford complete protection. With either of the other lamps it is apparent that for this series five minutes is near the threshold, but even with the higher energy the mercury bulb lamp failed to give as good protection as in series 2.

Series 5 (*Table 5*).—The following year, beginning on January 12, a fifth series of experiments was undertaken. The quartz mercury bulb lamp (fourth model), the air-cooled quartz mercury vapor arc lamp (third model) and the mercury vapor glow lamp (second model) were used, with only two minute and ten minute exposures. Also, it seemed advisable to determine whether the age of the subjects would affect the results. Therefore, slightly older rats were used.

For this reason the ratio of growth was lower in the normal group particularly and in many of the experimental groups than in the other series. The greatest average weight was attained in group 6, but since this group also had the greatest initial average, this is probably of little significance. As usual, the groups on the McCollum diet in general made the best showing when there was sufficient difference to justify the drawing of conclusions. However, the occurrence of rickets in one rat in group 10 and the slightly better growth in the rats in groups 5 and 15 than in the corresponding groups on the McCollum diet seem to represent definite exceptions to this rule.

A comparison of the averages of the final weights of the rats in all the groups exposed to each lamp shows the mercury bulb lamp (third model) to be decidedly inferior in regard to the promotion of growth; the air-cooled mercury vapor lamp (third model) and the mercury vapor glow lamp (second model) were of about equal efficiency. The energy incidence was 143×10^{-4} calories for the latter lamp (a newer model than that used in series 4). Since the two minute exposure was sufficient to protect against rickets in all other groups, it appears that some other factor must have been involved in the failure to protect all of the members of group 10. Consequently, there can be no conclusion as to comparative antirachitic value in this series.

SUMMARY OF THE PROTECTIVE VALUE OF VARIOUS LAMPS

Exposures for One Minute Daily.—To summarize all the work up to this point, the two lamps used in series 1, the carbon arc projector lamp and the small air-cooled quartz mercury vapor arc lamp, were efficiently protective but did not promote growth. With exposures of one minute the water-cooled quartz mercury arc lamp gave good protection but did not stimulate growth as well as the mercury bulb lamp (first model) which gave no protection.

TABLE 5 (Series 5).—*Duplicate Groups of Rats on the McCollum and Steenbock Diets Treated for Seven Weeks, Beginning January 12, with a Quartz Mercury Bulb Lamp at 15 Inches, an Air-Cooled Quartz Mercury Vapor Lamp at 21 Inches and a Mercury Vapor Glow Lamp at 10 Inches*

Group	No. of Rats	Average Initial Weight, Gm.	Average Maximum or Terminal Weight, Gm.	Growth Ratio	Exposure Time, Minutes		Calories per Square Centimeter per Minute	Lamp	Diet	Rickets
					Daily	Total				
1 (Controls)	8	60	171	1.85	..	.....	.....	.....	Wistar	None
2 (Controls)	8	63	119	0.88	..	.....	.....	.....	McCollum	Moderate
3 (Controls)	8	63	114	0.81	..	.....	.....	.....	Steenbock	Severe
4	4	63	110	0.75	2	98	67×10^{-4}	Mercury bulb, third model	McCollum	Slightly less than in group 2
5	4	59	117	1.00	2	98	61×10^{-4}	Mercury bulb, third model	Steenbock	Slightly less than in group 3
6	4	66	131	0.98	2	98	143×10^{-4}	Mercury vapor glow, second model	McCollum	Complete protection
7	4	62	103	0.66	2	98	143×10^{-4}	Mercury vapor glow, second model	Steenbock	Complete protection
8	4	57	114	1.00	2	98	155×10^{-4}	Air-cooled mercury vapor, third model	McCollum	Complete protection
9	3	60	118	0.96	2	98	155×10^{-4}	Air-cooled mercury vapor, third model	Steenbock	Complete protection
10	3	63	117	0.87	10	490	67×10^{-4}	Mercury bulb, third model	McCollum	Mild
11	3	55	101	0.84	10	490	67×10^{-4}	Mercury bulb, third model	Steenbock	Complete protection
12	4	61	126	1.07	10	490	143×10^{-4}	Mercury vapor glow, second model	McCollum	Complete protection
13	4	61	116	0.90	10	490	143×10^{-4}	Mercury vapor glow, second model	Steenbock	Complete protection
14	4	59	115	0.95	10	490	155×10^{-4}	Air-cooled mercury vapor, third model	McCollum	Complete protection
15	4	61	123	1.01	10	490	155×10^{-4}	Air-cooled mercury vapor, third model	Steenbock	Complete protection

Exposures for Two Minutes Daily.—The quartz mercury bulb lamp (second model, daily energy incidence of 36×10^{-4} calories) did not give any protection and did not appreciably stimulate growth, whereas the air-cooled mercury vapor lamp (second model, daily incidence of 71.6×10^{-4} calories) gave some protection and promoted growth. But with a daily energy incidence of 310×10^{-4} calories there was only a slightly better showing with this lamp.

With a daily energy incidence of 40.2×10^{-4} calories the mercury bulb lamp (first model) did not greatly stimulate growth and afforded no protection. At 124×10^{-4} calories there was some antirachitic action but again no significant stimulation of growth.

The mercury vapor glow lamp (second model) for the same period (daily energy incidence of 286×10^{-4} calories) did not promote growth —in fact, in the group of rats on the Steenbock diet there was definite inhibition—but gave complete protection against rickets.

Exposures for Five Minutes Daily.—The water-cooled quartz mercury vapor arc lamp increased the rate of growth somewhat and, as with one minute exposures, gave complete protection against rickets.

The quartz mercury bulb lamp (second model, 90×10^{-4} calories) increased the rate of growth somewhat, especially in the McCollum group, but offered no protection.

The air-cooled mercury vapor arc lamp (second model, 169×10^{-4} calories) did not affect the rate of growth but gave complete protection. The later (third model, 775×10^{-4} calories) did not greatly accelerate the rate of growth but did protect to a considerable degree.

The mercury bulb lamp (first model, 100.5×10^{-4} calories) in series 2 accelerated growth and protected completely against rickets. In series 3, however, the same application seems to have retarded growth and did not protect the group on the Steenbock diet. It only partially protected the group on the McCollum diet. However, a new lamp of this design, with the same time but with a greater output of energy (third model, 335×10^{-4} calories) gave only slightly better protection and did not promote growth to any greater degree.

The mercury vapor glow lamp (first model, 585×10^{-4} calories) definitely increased both the rate of growth and the antirachitic action, although the degree of protection was not perfect.

Exposures for Ten Minutes Daily.—The air-cooled mercury vapor lamp for ten minutes daily (third model, $1{,}550 \times 10^{-4}$ calories) gave complete protection, but did not greatly improve growth. The mercury bulb lamp (third model, 670×10^{-4} calories) did not affect the rate of growth but gave nearly complete protection. The mercury vapor glow lamp (second model, $1{,}430 \times 10^{-4}$ calories) protected completely and improved the rate of growth to some extent.

Exposures for Thirty Minutes Daily.—The water-cooled mercury vapor lamp with exposures for thirty minutes daily gave complete protection and further improved the rate of growth over the one minute and five minute exposures.

The quartz mercury bulb lamp (second model, 540×10^{-4} calories) in series 2 gave little stimulation of growth. In series 3 the rate of growth was not greatly improved and little protection was apparent.

The smaller air-cooled mercury vapor lamp (second model, $1,074 \times 10^{-4}$ calories) gave complete protection, but the rate of growth was

TABLE 6 (Series 6).—*Duplicate Groups of Rats That Had Been Fed a Rachitogenic Diet for Five Weeks Treated for Seven Weeks with a Mercury Vapor Glow Lamp (First Model)*

Group	No. of Rats	Average Initial Weight, Gm.	Average Pretreatment Weight, Gm.	Average Maximum or Terminal Weight, Gm.	First Growth Ratio*	Second Growth Ratio	Daily Exposure Time, Minutes	Diet	Final Condition
1 (Controls)	4	39	161	220	4.60	0.360	..	.....	Normal
2 (Controls)†	5	41	54	64	0.56	0.185	..	McCollum	Very severe rickets
3 (Controls)	5	34	68	56	0.43	.....	..	Steenbock	Very severe rickets
4	4	40	63	75	0.87	0.190	3	McCollum	Complete healing
5	4	41	56	80	0.95	0.420	3	Steenbock	Complete healing
6	4	39	68	95	1.43	0.390	10	McCollum	Complete healing
7	4	40	64	76	0.90	0.190	10	Steenbock	Complete healing
8	4	37	60	98	1.50	0.630	20	McCollum	Complete healing
9	4	39	53	58	0.48	0.090	20	Steenbock	Complete healing
10†	..	41	60	96	1.34	0.600			

* The first growth ratio is based on the total gain in weight during the entire experiment; the second, on the gain made during the time that treatment was given with a mercury vapor glow lamp over the weight at the beginning of treatment.

† At the end of the second week of treatment two rats were removed from group 2 and were designated as group 10. See text for further details.

slightly less than for the rachitic controls. In series 4 (third model, $4,650 \times 10^{-4}$ calories) the rate of growth was not improved but complete protection was attained.

The mercury bulb lamp (first model) gave complete protection in three series and the rate of growth was always markedly improved.

The mercury vapor glow lamp (first model) in one series ($3,510 \times 10^{-4}$ calories) definitely improved the rate of growth and gave complete protection.

Only after three hours did the mercury bulb lamp (second model) bring about nearly complete protection, but with a rate of growth closely comparable to that of the group exposed to the same lamp for only thirty minutes.

THE CURATIVE VALUE OF VARIOUS LAMPS

In all the work up to this point the study was confined to the *protective* action of the various agencies. In another series the *curative* action of the mercury vapor glow lamp only was studied.

Series 6 (*Table 6*).—In this series the rats were placed on rachitogenic diets for five weeks. At the end of that time selected members of various groups were examined roentgenographically for evidence of rickets. Treatment was then given to duplicate groups for seven weeks. The average weight of the rats at the beginning of the experiments was 39.6 Gm. Exclusive of the normal controls the average weight at the beginning of treatment was 60.7 Gm. There were many deaths in this series. After three weeks of treatment the rats were again examined roentgenographically, and a third examination was made at the end of the experiment. Three roentgenologic reports, three weights and two weight ratios are included in the summaries. The first ratio is based on the total gain; the second, on the gain during the period of treatment over the weight at the beginning of treatment. The first figure shows the initial weight, the second shows the weight at the beginning of treatment and the third shows the final or maximum weight.

Only the mercury vapor glow lamp (first model) was used in this series (energy incidence, 120×10^{-4} calories per square centimeter per minute). In the normal control rats (group 1) the second ratio is low, indicating that growth was practically complete by the time that treatment was started.

In group 2 (the rachitic control rats on the McCollum diet) one rat died during the third week after treatment of the other groups was begun. At the end of the second week of the period of treatment, two rats were removed from this group and were thereafter designated as group 10, to be discussed later. The roentgenograms of the rats on the rachitogenic diet taken at the end of five weeks showed the presence of severe rickets. A second examination three weeks later showed the same condition, as did also the final examination of the two remaining members of the group.

In group 3 one rat died during the second week after the rachitogenic diet was begun, three died during the second week after treatment was begun, and the last rat died two weeks later. All roentgenographic examinations showed a severe rachitic condition.

In group 5 the preliminary roentgenogram showed severe rickets in all of the rats, but after three weeks two rats showed nearly complete healing, the two others having made little improvement. One of the latter died shortly afterward, the other during the fourth week. The survivors showed complete healing at the final examination.

In group 8 the first roentgenogram showed the presence of rickets and two of the rats died during the first week of treatment. The two rats comprising group 10, which had been removed from group 2 at the end of six weeks when roentgenograms showed the presence of severe rickets, were exposed for thirty minutes daily to the lamp with a chlorine-bromine filter interposed. This restricted the spectrum to rays of shorter wavelength than 2,800 angstroms and reduced the energy incidence from 120×10^{-4} to 25×10^{-4} calories. Table 7 shows the extent of the modification of the spectral distribution. The total daily energy incidence was 750×10^{-4} with 667.5×10^{-4} calories per day from the region below 2,550 angstroms. Healing was complete and growth was practically equal to that in the best of the experimental groups of this series (groups 6 and 8).

TABLE 7.—*The Percentage of the Distribution of Energy in Various Spectral Fields for Seven Lamps*

Lamp	Percentage of Distribution of Energy		
	Less Than 2,550 Angstroms	2,550 to 3,000 Angstroms	3,000 to 3,350 Angstroms
Air-cooled quartz mercury vapor, second model....	40	35	25
Air-cooled quartz mercury vapor, third model.....	55	32	13
Mercury bulb, first model.....	5	50	45
Mercury bulb, third model.....	26	51	23
Mercury bulb, second model.....	0	10	90
Mercury vapor glow, first model.....	84	15	1
Mercury vapor glow, first model with gas filter.....	89	11	0

TABLE 8.—*The Distribution of Energy in Three Spectral Ranges in Calories per Square Centimeter per Day*

Lamp	Series	Group	Less Than 2,550 Angstroms	2,550 to 3,000 Angstroms	3,000 to 3,350 Angstroms	Total Calories per Day
Air-cooled quartz						
mercury vapor,	3	11, 12	28.640×10^{-4}	25.06×10^{-4}	17.900×10^{-4}	71.6×10^{-4}
second model		13, 14	71.600×10^{-4}	62.65×10^{-4}	44.750×10^{-4}	179.0×10^{-4}
Air-cooled quartz	4	15, 16	429.600×10^{-4}	375.90×10^{-4}	268.500×10^{-4}	$1,074.0 \times 10^{-4}$
mercury vapor,		5, 6	426.250×10^{-4}	248.00×10^{-4}	100.750×10^{-4}	775.0×10^{-4}
third model		11, 12	$2,557.500 \times 10^{-4}$	$1,488.00 \times 10^{-4}$	604.500×10^{-4}	$4,650.0 \times 10^{-4}$
	5	8, 9	170.500×10^{-4}	99.20×10^{-4}	40.300×10^{-4}	310.0×10^{-4}
		14, 15	852.500×10^{-4}	496.00×10^{-4}	201.500×10^{-4}	$1,550.0 \times 10^{-4}$
Mercury bulb,	2	3	1.005×10^{-4}	10.05×10^{-4}	9.045×10^{-4}	20.1×10^{-4}
first model		6	5.025×10^{-4}	50.25×10^{-4}	45.225×10^{-4}	100.5×10^{-4}
		9	30.150×10^{-4}	301.50×10^{-4}	271.350×10^{-4}	603.0×10^{-4}
	3	5, 6	2.010×10^{-4}	20.10×10^{-4}	18.090×10^{-4}	40.2×10^{-4}
		7, 8	5.025×10^{-4}	50.25×10^{-4}	45.225×10^{-4}	100.5×10^{-4}
		9, 10	30.150×10^{-4}	301.50×10^{-4}	271.350×10^{-4}	603.0×10^{-4}
Mercury bulb,	4	3, 4	87.100×10^{-4}	170.85×10^{-4}	77.050×10^{-4}	335.0×10^{-4}
third model		9, 10	522.600×10^{-4}	$1,025.10 \times 10^{-4}$	462.300×10^{-4}	$2,010.0 \times 10^{-4}$
	5	4, 5	34.840×10^{-4}	68.34×10^{-4}	30.820×10^{-4}	134.0×10^{-4}
		10, 11	174.200×10^{-4}	341.70×10^{-4}	154.100×10^{-4}	670.0×10^{-4}
Mercury bulb,	2	4	Trace	3.60×10^{-4}	32.400×10^{-4}	36.0×10^{-4}
second model		7	Trace	54.00×10^{-4}	486.000×10^{-4}	540.0×10^{-4}
		10	Trace	324.00×10^{-4}	$2,916.000 \times 10^{-4}$	$3,240.0 \times 10^{-4}$
	3	17, 18	Trace	9.00×10^{-4}	81.000×10^{-4}	90.0×10^{-4}
		19, 20	Trace	54.00×10^{-4}	486.000×10^{-4}	540.0×10^{-4}
Mercury vapor	4	7, 8	491.400×10^{-4}	87.75×10^{-4}	5.850×10^{-4}	585.0×10^{-4}
glow, first model		13, 14	$2,948.400 \times 10^{-4}$	526.50×10^{-4}	35.100×10^{-4}	$3,510.0 \times 10^{-4}$
Mercury vapor	5	6, 7	240.240×10^{-4}	$42.90 \times 10^{4-}$	2.860×10^{-4}	286.0×10^{-4}
glow, second model		12, 13	$1,201.200 \times 10^{-4}$	214.50×10^{-4}	14.300×10^{-4}	$1,430.0 \times 10^{-4}$
	6	4, 5	302.400×10^{-4}	54.00×10^{-4}	3.600×10^{-4}	360.0×10^{-4}
		6, 7	$1,008.000 \times 10^{-4}$	180.00×10^{-4}	12.000×10^{-4}	$1,200.0 \times 10^{-4}$
		8, 9	$2,016.000 \times 10^{-4}$	360.00×10^{-4}	24.000×10^{-4}	$2,400.0 \times 10^{-4}$
		10	667.500×10^{-4}	82.50×10^{-4}	Trace	750.0×10^{-4}

In every group in series 6 that received treatment all the rats that survived showed complete healing of the rachitic lesions. During the period of treatment the best growth was shown by groups 6, 8 and 10. The ten and twenty minute exposures actually seemed to inhibit growth in groups 7 and 9 when compared to group 5, which showed the best rate of growth of any of the groups of rats on the Steenbock diet that received treatment. This same tendency is seen in some of the other groups, i. e., retarding of growth by too prolonged exposure.

THE COMPARATIVE VALUE OF VARIOUS SPECTRAL RANGES

An attempt was next made to determine the comparative value of the spectral ranges indicated in table 7. This table shows the percentage of the total energy for each lamp distributed in each of three spectral ranges. Table 8 was constructed by the use of these percentages to determine the actual energy application per day in each range.

When the actual daily energy incidences (table 9) in the range below 2,550 angstroms were arranged in the order of increasing intensity, irrespective of the source, and the antirachitic effects were correlated, it was found that with all ranges within which there was a negligible incidence of energy in this region, there was little protection in all groups and generally poor growth. However, in the range from 1×10^{-4} to 10×10^{-4} calories per day there was complete protection in one group and poor protection in the other, with fair and with good growth, respectively.

In ranges between 10×10^{-4} and 100×10^{-4} calories per day there was practically no consistent conformity, but above that range twenty-two of a total of twenty-nine groups showed complete protection. There was also generally good growth. However, there were enough failures even in the higher ranges of energy incidence to suggest that the radiations have little to do, directly, with the rate of growth. The slow growth in the lower ranges is probably a reflection of a general poor condition of nutrition.

In table 10 figures for daily energy incidence in the ranges below 2,550 and from 2,550 to 3,000 angstroms combined are arranged in ascending order. While there was some rearrangement in the position of certain groups, there was no significant change in the relationship to the antirachitic effect or to the promotion of growth. Only small antirachitic effects were noticeable below 50×10^{-4} calories per day. Above 700×10^{-4} calories there was practically always complete protection. In a general way there was perhaps better correlation between the magnitude of the energy incidence and the growth than in table 9. The rate of growth was generally poor below 50×10^{-4} and generally good above 300×10^{-4} calories.

TABLE 9.—*Summary of the Antirachitic and Growth Effects Arranged in the Order of Increasing Intensity of Energy in the Range Below 2,550 Angstroms, Irrespective of the Source*

Calories per Square Centimeter per Day	Series	Groups: McCollum Diet	Groups: Steenbock Diet	Antirachitic Protection	Growth
Trace	2	4	..	None	Very poor
		7	..	None	Poor
		10	..	Fair	Good
	3	17	..	Slight	Fair
			18	Slight	Poor
		19	..	Fair	Good
			20	Slight	Poor
1×10^{-4} to 10×10^{-4}	2	3	..	Poor	Fair
		6	..	Complete	Good
	3	5	..	Moderate	Good
			6	Poor	Poor
		9	..	Complete	Very good
			10	Very good	Good
	2	9	..	Complete	Fair
	5	4	..	Slight	Poor
			5	Slight	Fair
	3	7	..	Good	Poor
			8	Poor	Poor
	4	3	..	Fair	Fair
			4	Good	Poor
10×10^{-4} to 50×10^{-4}	3	11	..	Good	Very good
			12	Good	Poor
	2	9	..	Complete	Fair
	3	9	..	Complete	Very good
			10	Very good	Good
	5	4	..	Slight	Poor
			5	Poor	Good
50×10^{-4} to 100×10^{-4}	3	13	..	Complete	Good
			14	Very good	Very good
	4	3	..	Fair	Fair
			4	Good	Very poor
100×10^{-4} to 200×10^{-4}	5	8	..	Complete	Good
			9	Complete	Good
		10	..	Good	Fair
			11	Complete	Fair
200×10^{-4} to 300×10^{-4}	5	6	..	Complete	Fair
			7	Complete	Very poor
300×10^{-4} to 400×10^{-4}	6	4	..	Complete	Poor
			5	Complete	Fair
400×10^{-4} to 500×10^{-4}	4	5	..	Good	Good
			6	Good	Fair
	3	15	..	Complete	Moderate
			16	Complete	Poor
	4	7	..	Very good	Good
			8	Very good	Fair
500×10^{-4} to 600×10^{-4}	4	9	..	Very good	Good
			10	Good	Fair
600×10^{-4} to 700×10^{-4}	6	10	..	Complete	Very good
700×10^{-4} to $1,000 \times 10^{-4}$	5	14	..	Complete	Good
			15	Complete	Good
$1,000 \times 10^{-4}$ to $2,000 \times 10^{-4}$	6	6	..	Complete	Very good
			7	Complete	Fair
	5	12	..	Complete	Good
			13	Complete	Good
$2,000 \times 10^{-4}$ to $3,000 \times 10^{-4}$	6	8	..	Complete	Very good
			9	Complete	Very poor
	4	11	..	Complete	Fair
			12	Complete	Fair
		13	..	Complete	Very good
			14	Complete	Good

TABLE 10.—*Summary of the Antirachitic and Growth Effects Arranged in the Order of Increasing Intensity of Energy in the Ranges Below 2,550 Angstroms and from 2,550 to 3,000 Angstroms Combined*

Calories per Square Centimeter per Day	Series	Groups: McCollum Diet	Groups: Steenbock Diet	Antirachitic Protection	Growth
1×10^{-4} to 10×10^{-4}	2	4	..	None	Very poor
		17	..	Slight	Fair
			18	Slight	Poor
10×10^{-4} to 50×10^{-4}	2	3	..	Poor	Fair
	3	5	..	Fair	Fair
			6	Poor	Poor
50×10^{-4} to 100×10^{-4}	2	6	..	Complete	Good
	3	7	..	Good	Fair
			8	Slight	Poor
	2	7	..	None	Poor
	3	11	..	Good	Very good
			12	Good	Poor
		19	..	Fair	Good
			20	Poor	Fair
100×10^{-4} to 200×10^{-4}	5	4	..	Slight	Poor
			5	Poor	Good
	3	13	..	Complete	Good
			14	Very good	Very poor
		8	..	Complete	Good
			9	Complete	Good
200×10^{-4} to 300×10^{-4}	4	3	..	Fair	Fair
			4	Good	Poor
	5	6	..	Complete	Fair
			7	Complete	Very poor
300×10^{-4} to 400×10^{-4}	2	9	..	Complete	Fair
		10	..	Fair	Good
	3	9	..	Complete	Very good
			10	Very good	Good
	6	4	..	Complete	Poor
			5	Complete	Fair
500×10^{-4} to 600×10^{-4}	5	10	..	Good	Fair
			11	Complete	Fair
	4	7	..	Very good	Good
			8	Very good	Fair
600×10^{-4} to 700×10^{-4}	4	5	..	Good	Good
			6	Good	Fair
700×10^{-4} to $1,000 \times 10^{-4}$	3	15	..	Complete	Moderate
			16	Complete	Poor
	6	10	..	Complete	Very good
$1,000 \times 10^{-4}$ to $2,000 \times 10^{-4}$	5	14	..	Complete	Good
			15	Complete	Good
	4	9	..	Very good	Good
			10	Good	Fair
	5	12	..	Complete	Good
			13	Complete	Good
	6	6	..	Complete	Very good
			7	Complete	Fair
$2,000 \times 10^{-4}$ to $3,000 \times 10^{-4}$	6	8	..	Complete	Very good
			9	Complete	Very poor
$3,000 \times 10^{-4}$ or more	6	11	..	Complete	Fair
			12	Complete	Fair
		13	..	Complete	Very good
			14	Complete	Good

COMMENT

In a paper by Clark and Mrgudich [1] are shown the results of a study of certain selected bones from some of our animals by roentgen ray diffraction patterns. This field of study offers interesting possibilities and should be extended further.

The generally less favorable showing of the animals on the Steenbock diet is difficult to explain. Theoretically the Steenbock diet has a calcium-phosphorus ratio of 4.25 and the McCollum diet a ratio of 4.04. However, this difference is probably not the important factor. Aside from possible varying amounts of vitamin A in the yellow cornmeal, the McCollum diet contains 33 per cent whole wheat and this might contain more provitamin D. The actual biologic value of the particular rachitogenic diet used must receive more consideration in all future experiments of this nature.

The fact that there is not complete quantitative parallelism between the energy incidence and the therapeutic effects indicates clearly the existence of an extremely wide threshold range and suggests an explanation for the discrepancies in the results obtained by different workers who have attempted to establish a therapeutic threshold. In view of our results, it seems improbable that it will ever be possible to establish an absolute threshold; at least, this cannot be done until the underlying physiologic factors are better understood.

In general our results accord well with those of Sonne and Rekling,[2] who showed that good antirachitic effects may be obtained with wavelengths as low as 2,530 angstroms.

Clausen [3] and Ludwig and von Ries [4] have shown that visible and infra-red rays affect favorably the rates of growth of rachitic rats. We have seen little evidence in this series of any close correlation between the rate of growth and the energy incidence from these sources.

The effective wavelength for antirachitic action has been the subject of extensive investigation.[5] The marked protective effect obtained by the use of the filtered rays from the mercury vapor glow lamp (table 6, group 10), in which 89 per cent of the total energy incidence was in

1. Clark, G. L., and Mrgudich, J. N.: An X-Ray Diffraction Study of the Effect of Rachitis upon the Structural Characteristics of Bone, Am. J. Physiol. **108**:74 (April) 1934.

2. Sonne, C., and Rekling, E.: Behandlung experimenteller Rattenrachitis mit monochromatischem ultraviolettem Licht, Strahlentherapie **25**:552, 1927.

3. Clausen, E. M. L.: The Use of Isolated Radiations in Experiments with the Rat: I. The Effect of Infra-Red Radiation on the Growth of the Rachitic Rat, J. Nutrition **2**:125 (Nov.) 1929.

4. Ludwig, F., and von Ries, J.: Ueber den Einfluss der Rot- und Blaustrahlen auf das Wachstum, Strahlentherapie **39**:485, 1931.

5. Laurens, H.: The Physiological Effects of Radiant Energy, New York, The Chemical Catalog Company, 1933.

the region below 2,550 angstroms, demonstrates clearly that the short rays are even more effective than Sonne and Rekling believed them to be.[6]

CONCLUSIONS

1. The relation of the source of radiant energy to the degree of antirachitic and growth-promoting effects in rats on rachitogenic diets has been investigated.

2. Animals on the Steenbock diet offer a more rigid test of radiation therapy than those on the McCollum diet.

3. Good antirachitic effects may be obtained from rays with a wavelength as low as 2,550 angstroms.

4. The factors responsible for the promotion of growth are not determinable by this method.

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6. Bachem, A.: Physiology of the Mercury Line 254 mμ, Arch. Phys. Therapy **13**:614 (Oct.) 1932.

EFFECT OF IRON AND COPPER THERAPY ON HEMOGLOBIN CONTENT OF THE BLOOD OF INFANTS

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In a recent study by Elvehjem, Peterson and Mendenhall [1] on the hemoglobin content of the blood of seven hundred and fifty infants varying in age from birth to 5 years, it was shown that the average value for children from 6 months to 2½ years of age was between 11 and 12 Gm. per hundred cubic centimeters. Since these children were from different kinds of homes it was impossible to determine whether the low figure for hemoglobin at that age was a normal condition or was due to a dietary deficiency. A definite answer can be made only when a study is made of children known to be receiving ample supplies of blood-forming elements. In this report we present values for hemoglobin obtained with children receiving, in addition to their regular diet, known amounts of iron and copper salts.

The children studied were healthy infants brought to the Dudgeon School Clinic, one of the child health centers of the Madison Public Health Nursing Association. Any child whose mother was willing to cooperate in the study was used, but a special effort was made to select subjects particularly from the younger group of infants coming to the clinic, so that the administration of salts could be started as early as possible. The ages of the children observed in this study ranged from 3 weeks to 1 year or over.

The method of collecting samples of blood and of determining the values for hemoglobin was the same as that used in the earlier work.[1] All the values are reported in grams per hundred cubic centimeters of blood. One or more determinations were made before the iron and copper were added to the diet. Additions were made to the diets of infants with a low hemoglobin content of the blood and of very young

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1. Elvehjem, C. A.; Peterson, W. H., and Mendenhall, D. R.: Hemoglobin Content of the Blood of Infants, Am. J. Dis. Child. **46**:105 (July) 1933.

infants; in the case of the latter it was hoped that the addition of iron and copper salts would prevent the drop in hemoglobin content which is characteristic at the ages of 2 and 3 months.

The majority of infants received the iron and copper either in the form of a solution or as tablets. The liquid consisted of a solution of powdered ferric pyrophosphate, $Fe_4(P_2O_7)_3$, and copper sulphate, $CuSO_4$. Ferric pyrophosphate was selected because, being readily soluble, odorless and tasteless and devoid of great astringent properties, it is fairly easily administered. Feeding experiments with rats [2] have shown that in this form the iron is readily available. The iron and copper solution was prepared by dissolving 10 Gm. of ferric pyrophosphate and 0.4 Gm. of copper sulphate in 250 cc. of distilled water containing 5 per cent alcohol. One teaspoonful (5 cc.) was given daily by incorporating it in the infant's formula or orange juice or in a glass of milk in the case of older children. In each teaspoonful the child received 25 mg. of elemental iron and 1 mg. of elemental copper.

The tablets used in the study contained ferric pyrophosphate and copper sulphate in amounts sufficient to furnish in each tablet 25 mg. of elemental iron and 1 mg. of elemental copper. One tablet was given daily, being administered in the infant's formula or in a glass of milk, in which it was found to dissolve readily.

No partiality was shown in recommending one or the other form of iron and copper preparation. An effort was made to have approximately the same number of children use each kind, but this did not prove feasible, as it was not always possible to continue determinations of hemoglobin on each child. Of the fifty-five children studied, thirty-seven received the iron and copper solution; ten received the tablets, and eight received miscellaneous forms of iron and copper.

RESULTS

The results of the study with the iron and copper salts are illustrated in the accompanying charts. In each the solid line is constructed from the average results of determinations of hemoglobin made on children receiving no iron therapy. It differs from the curve given in our previous paper in that it includes averages for all the children admitted to the clinic, regardless of whether they were anemic or not. The earlier curve excluded the figures for twins and children who appeared definitely anemic.

The broken line pictures the figures obtained from determinations of hemoglobin made on children receiving iron and copper therapy. All

2. Elvehjem, C. A.; Hart, E. B., and Sherman, W. C.: The Availability of Iron from Different Sources for Hemoglobin Formation, J. Biol. Chem. **103**:61 (Nov.) 1933.

the curves show results in individual cases, except the curve given in chart 3, which shows average results. The crosses indicate the points at which increases in the amounts of iron and copper were made.

Iron and Copper Solution.—The infants receiving the iron and copper solution showed in most instances a definite rise in the hemoglobin content. Curves for representative cases which are typical of the results are shown in chart 1. In case 3 there was a fall in hemoglobin content from 11.5 Gm. to slightly over 10.5 Gm. between the ages of 16 and 22 weeks. At that point the administration of iron and copper solution was begun, and in four weeks the content rose to 12.5 Gm. Determinations made at the ages of 32 and 38 weeks showed values approximating 12.8 Gm.

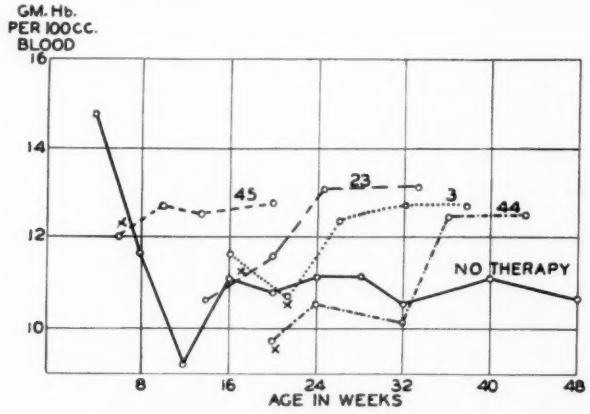

Chart 1.—Curves showing the hemoglobin content for four infants receiving 25 mg. of iron and 1 mg. of copper daily as a solution of the salts. The numbers designate the individual cases.

In case 23 at 14 weeks the child showed a hemoglobin level well below 11 Gm. The iron and copper solution was administered three weeks later. The hemoglobin content increased to 11.5 Gm. at the age of 20 weeks and to slightly over 13 Gm. at 25 weeks. A determination made nine weeks later gave a similar value.

In case 44 the child began taking the solution at the age of 20 weeks, when the hemoglobin level was below 10 Gm. The content rose slightly in the next four weeks but fell again and was barely over 10 Gm. at 32 weeks. After that it rose abruptly to 12.5 Gm. and remained at that level at the forty-third week.

In case 45 the child was given the solution at 6 weeks of age, when the first determination of hemoglobin was made. Instead of showing the subsequent fall usually observed at that age the hemoglobin content rose in four weeks from slightly over 12 to 12.8 Gm., and it remained at approximately that level for the following ten weeks.

Iron and Copper Tablets.—The results with the tablets showed in most cases a definite rise in the hemoglobin content, as illustrated by four representative curves given in chart 2. In case 36 the child began to take the tablets at 11 weeks; a test at 10 weeks had shown the hemoglobin level to be about 10.5 Gm. At the fourteenth week the content had risen to well over 12 Gm.; it remained constant for six weeks and then rose slightly at the twenty-third week to a level of about 13 Gm.

In case 38 at 30 weeks the child showed a hemoglobin level below 9.5 Gm. The tablets were administered at 34 weeks, with a resultant rise in the hemoglobin content to slightly over 12 Gm. at 40 weeks and to nearly 13 Gm. at 48 weeks.

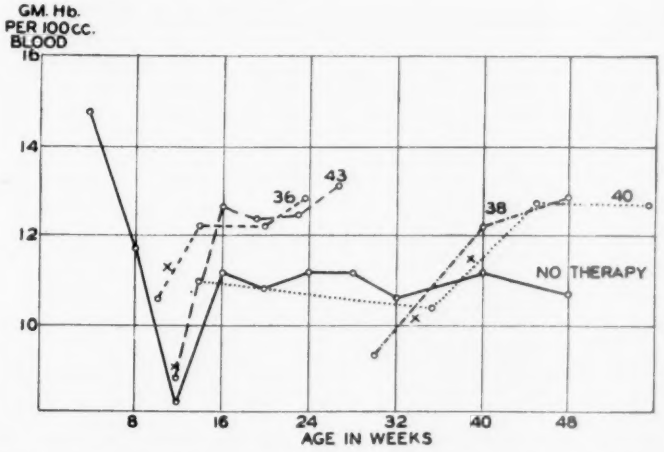

Chart 2.—Curves showing the hemoglobin content for four infants receiving 25 mg. of iron and 1 mg. of copper daily in the form of tablets. The numbers designate the individual cases.

In case 40 a fall in the hemoglobin content from 11 Gm. to below 10.5 Gm. occurred when the child was 35 weeks old. The tablets were started at 39 weeks, and the therapy was followed by a rise in the content to approximately 12.8 Gm. at 45 and at 55 weeks.

In case 43 an abrupt rise occurred in four weeks from below 9 Gm. to 12.5 Gm. at 16 weeks. The hemoglobin remained at this level for the next eleven weeks and finally increased to 13 Gm. or over.

The average results for all the infants receiving 25 mg. of iron and 1 mg of copper are given in chart 3. The average value before therapy remained at about 11 Gm., but in infants receiving the iron and copper the hemoglobin content increased to approximately from 12 to 12.5 Gm. The characteristic drop at 8 weeks was not prevented by the addition of the salts. However, a study of the curve in chart 3 and of the individual curves in charts 1 and 2 shows that in most

cases the decrease in hemoglobin at this point was greatly reduced. The average curve for the infants receiving iron and copper was higher at every point after 8 weeks of age than the average curve for the untreated infants.

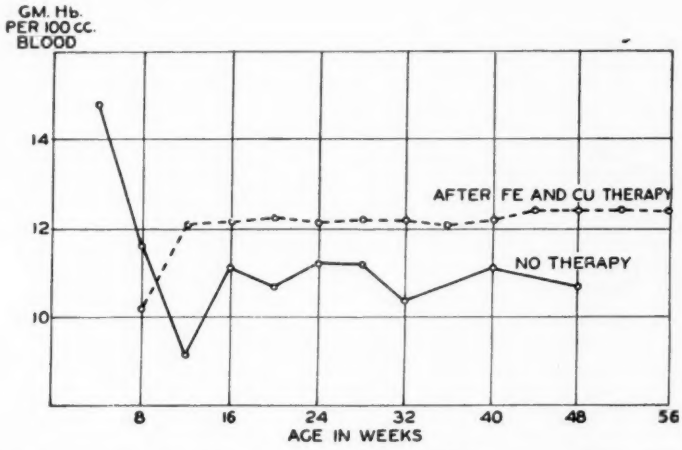

Chart 3.—Curves showing the average hemoglobin content for forty-seven infants receiving 25 mg. of iron and 1 mg. of copper daily.

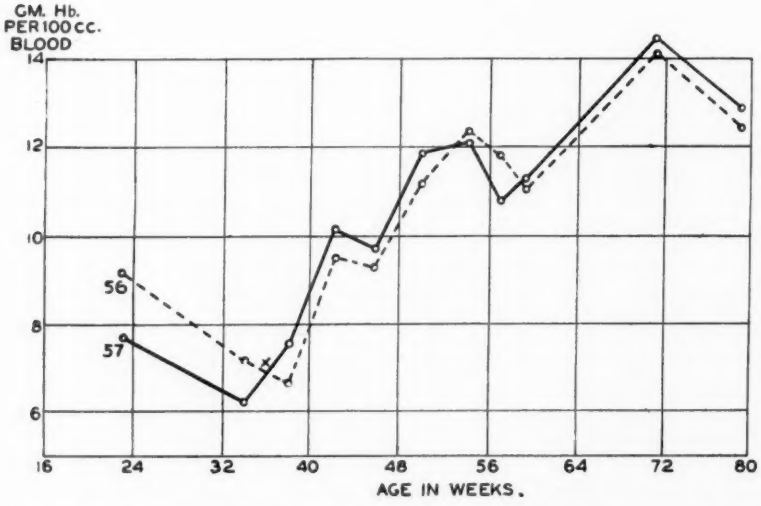

Chart 4.—Curves showing the hemoglobin content for two severely anemic infants receiving 25 mg. of iron and 1 mg. of copper daily.

The changes in the hemoglobin content in two (twins) severely anemic infants who received 25 mg. of iron and 1 mg. of copper in the form of a solution is given in chart 4. It is readily seen that a fairly rapid response is obtained with this amount of iron and copper

even in infants with very low hemoglobin levels. Smaller doses of iron and copper are less satisfactory. Several infants given daily 12.5 mg. of iron and 0.5 mg. of copper showed considerable response, but the effect was not as uniform as with the higher doses. An interesting case is illustrated in chart 5 (case 32). The iron and copper therapy was begun at 8 weeks of age, when the hemoglobin was approximately 11.5 Gm. Two weeks later the content had dropped to 10.5 Gm., but then it showed an abrupt rise to 13.5 Gm., remaining at that level for the following nine weeks. It fell to 10.3 and 9.5 Gm. at 26 and 29 weeks. A slight digestive disturbance may have been the cause of the rapid drop in hemoglobin. There was a gradual increase during the following seven weeks, and the former levels were reached at 36 weeks

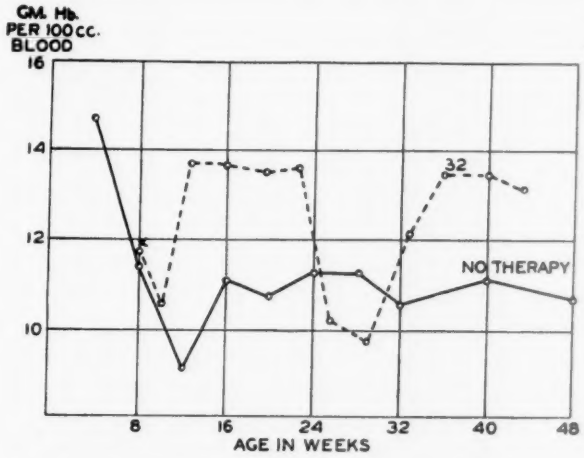

Chart 5.—Curves showing the hemoglobin content for an infant receiving 12.5 mg. of iron and 0.5 mg. of copper daily.

of age. Although one cannot be sure that a larger dose of iron and copper would have prevented this sudden drop, similar fluctuations were not observed in infants receiving the larger amounts of the metals.

COMMENT

The results presented in this paper demonstrate that the normal curve for the hemoglobin content of the blood of infants is somewhat higher than the average curve presented in our earlier paper. We are probably safe in concluding that the normal hemoglobin content of the blood of infants between the ages of 3 months and 1 year should be between 12 and 13.5 Gm. per hundred cubic centimeters. Our figures are slightly higher than the revised values given by Mackay [3] for the

3. Mackay, H. M. M.: The Normal Haemoglobin Level During the First Year of Life: Revised Figures, Arch. Dis. Childhood **8**:221 (June) 1933.

normal level during the first year of life. However, the small remaining difference is undoubtedly due to the use of different instruments. That values between 12 and 13.5 Gm. are normal is further substantiated by the individual records. Practically all the curves flatten out on that level after iron and copper therapy. Mackay has constructed her normal curve so that there is a gradual increase between the ages of 3 and 5 months. Our results show that if the iron and copper therapy is started very early the hemoglobin is increased to 12 Gm. or more by the third month. Although the degree of drop at 2 months of age can be reduced and the normal value can be attained by 3 months of age, the low level at 2 months cannot be completely eliminated even with the administration of iron and copper.

The fact that the values for practically all the untreated infants are lower than the values obtained after therapy forces us to conclude that a large number of children suffer from slight anemia. Whether this lowered hemoglobin content has any significance in the health and well-being of the children is difficult to determine. We have not had an opportunity to study this question, but Mackay and Goodfellow [4] have correlated the prevalence of children's diseases with a low hemoglobin content, and Kato and Emery [5] stated that there must be some relation between the low hemoglobin content and the degree of resistance against invading micro-organisms.

The readiness with which the children observed responded to iron and copper therapy indicates that the amount of these elements in their diet must have been on the borderline of an adequate supply. This is not surprising when one considers the relatively low iron and copper content of most of the foods used in diets for infants and also the fact that a considerable portion of the iron in the food is unavailable.[6]

Our results suggest that it may be advisable to add small amounts of iron and copper to the diets of some infants to insure an optimum formation of hemoglobin. There is no doubt that the most desirable form of iron is that which is in simple combination and is known to be readily available. There may be some question about the exact type of salt to be used, but we have found the pyrophosphate to be satisfactory. The amount administered may be very small; 25 mg. of iron daily is an ample supply. Even in the case of rather severe nutritional anemia the amount is sufficient to produce a rapid response (chart 4).

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4. Mackay, H. M. M., and Goodfellow, L.: Nutritional Anaemia in Infancy, Medical Research Council, Spec. Rep. Ser. 157, London, His Majesty's Stationery Office, 1931.

5. Kato, K., and Emery, O. J.: Hemoglobin Content of the Blood in Infancy, Folia haemat. **49**:106, 1933.

6. Elvehjem, C. A.; Hart, E. B., and Sherman, W. C.: The Limitations of Cereal-Milk Diets for Hemoglobin Formation, J. Pediat. **4**:65 (Jan.) 1935; footnote 2.

The cost of such additions to the diet should be very small. The amount of iron administered should be reduced to a minimum for other reasons. We have data (unpublished) showing that the ingestion of large amounts of iron interferes seriously with the assimilation of phosphorus and leads to severe rickets in growing animals. Often 500 mg. or more of iron is recommended; this amount may be equal to or even greater than the daily intake of phosphorus. The dosage of iron in cases of simple nutrition anemia must remain at a low level if one is to expect continued beneficial results from iron therapy.

Naturally the question of whether the iron must be administered with copper is a pertinent one. In this work we have reduced the amount of iron to a minimum and added definite amounts of copper to insure a proper utilization. It is true that an infant's diet containing cereals is less likely to be deficient in total copper than in iron. However, we have made a few studies using 25 mg. of iron alone, and in most cases the response to iron alone has been slower and less extensive than the response observed after both iron and copper were administered. The use of a small amount of copper and iron in the ratio of 1 : 25 is certainly superior in many ways to the use of excessive doses of iron alone. In a recent article by Cason [7] a ratio of copper to iron of 1 : 25 was recommended, but the amount administered in his experiments was from ten to twenty times as large as the amount we have used.

SUMMARY

1. The daily addition of 25 mg. of iron and 1 mg. of copper as ferric pyrophosphate and copper sulphate, respectively, in the form of a solution or of tablets to the regular diet of infants caused an increase in the hemoglobin content of the blood from between 9 and 11 Gm. to from 12 to 13.5 Gm. per hundred cubic centimeters.

2. The addition of smaller amounts of iron and copper (12.5 mg. of iron and 0.5 mg. of copper daily) did not give as uniform or consistent results as the use of larger doses of these elements.

3. A fairly rapid rise in the hemoglobin content of the blood of infants suffering from severe nutritional anemia was obtained by the daily administration of 25 mg. of iron and 1 mg. of copper.

4. The use of small amounts of simple iron and copper salts for the maintenance of optimum hemoglobin levels in growing infants is discussed.

Miss Irene Haan supplied some of the records of the hemoglobin content reported in this paper.

7. Cason, J. F.: The Use of Copper and Iron in the Treatment of Secondary Anemia in Children, J. Pediat. **4**:614 (May) 1934.

FILAMENTED-NONFILAMENTED CELL COUNT IN APPENDICITIS IN CHILDREN

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Few facts in medicine are as well established as the increase in leukocytes and neutrophils that characterizes certain infectious processes, although the information to be gained from a study of the morphologic characteristics of the leukocytes responsible for this increase has not received due consideration. In the development of an adult polymorphonuclear neutrophil, the young cell passes through a series of well defined stages, with gradually increasing condensation and segmentation of the nuclear chromatin and the appearance of granules and neutrophilic staining properties in the cytoplasm, until the mature neutrophil is formed. The observation that there is an increase in the number of the less mature polymorphonuclear neutrophils in certain acute infections is the basis for the various methods of classification of these cells which have appeared from time to time during the past thirty years.

Arneth [1] is credited with the pioneer work on the changes in nuclear structure of the neutrophil under various conditions. In 1904 he published his classification in which he divided these cells into five main groups, each corresponding to the number of segments in the nucleus. He noted the increase in the nonsegmented or less mature forms during acute infections. The complexity of his classification prevented its widespread adoption, and it was not until 1920 that Schilling [2] modified Arneth's system to a more practical form. He grouped each kind of leukocyte separately and then subdivided the neutrophils into four groups, three of which comprised cells with nonsegmented nuclei and the fourth, those in which the nuclear segments were joined by a thin, hairlike strand of chromatin known as a filament. In the order of their maturity the three types of nonsegmented forms were classified as myelocytes, with round nuclei, metamyelocytes, with indented nuclei, and band forms, with bilobed nuclei the segments of which were joined by a rather broad band of chromatin. Schilling called the increase in

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Work done in the Section on Pediatrics, The Mayo Clinic.

1. Arneth, J.: Die neutrophilen Leukozyten bei Infektionskrankheiten, Deutsche med. Wchnschr. **1**:54, 1904.

2. Schilling, V.: Nuclear Lobes in Neutrophil Leukocytes, Ztschr. f. klin. Med. **89**:1, 1920.

nonsegmented neutrophils a "shift to the left," indicative of a preponderance of younger cells released from the bone marrow in response to acute infection. He as well as Arneth noted the toxic changes in the neutrophils which occurred during acute infection, but he placed less emphasis on such changes.

The next modification in the classification of leukocytes was that advanced by Pons and Krumbhaar [3] in 1924. They classified neutrophils as those with indented nuclei (metamyelocytes), those in which the segments were connected by a broad band of chromatin and those in which the nuclear segments were joined by a fine filament of chromatin.

Cooke and Ponder [4] in 1927 presented a classification of neutrophils into five types, each type depending on the number of nuclear segments connected by filaments. Farley, St. Clair and Reisinger [5] in 1930 combined the two systems last mentioned into a more simple method by dividing the neutrophils found in the course of a regular differential leukocyte count into two groups: the filamented cells, in which the nuclear segments were joined by a fine thread of chromatin, and the nonfilamented forms, in which either the nuclear segments were joined by a broader mass of chromatin or the nuclei were nonsegmented. Since the increase in segmentation of the polymorphonuclear neutrophils indicates maturity, the nonfilamented group represents the younger forms. The nonfilamented forms were found to increase during the course of an acute infection, and if the number exceeded 16 per cent of the total leukocyte count it was considered to be above the normal values obtained for healthy adults.

Mullin and Large [6] in 1931 described a method by which they counted 100 neutrophils and divided them into filamented and nonfilamented forms. They expressed the belief that much prognostic significance may be attached to changes in the ratio of nonfilamented to filamented neutrophils. In their experience, a proportion of nonfilamented neutrophils greater than 50 per cent forced them to give a guarded prognosis.

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3. Pons, C., and Krumbhaar, E. B.: Studies in Blood Cell Morphology and Function: Extreme Neutrophilic Leucocytosis With Note on Simplified Arneth Count, J. Lab. & Clin. Med. **10**:123 (Nov.) 1924.

4. Cooke, W. E., and Ponder, Eric: The Polynuclear Count, Philadelphia, J. B. Lippincott Company, 1927.

5. Farley, D. L.; St. Clair, H., and Reisinger, J. A.: Normal Filament and Nonfilament Polymorphonuclear Neutrophil Count: Its Practical Value as Diagnostic Aid, Am. J. M. Sc. **180**:336 (Sept.) 1930.

6. Mullin, W. V., and Large, G. C.: The Filament-Nonfilament Count: Its Diagnostic and Prognostic Value, Tr. Sect. Laryng., Otol. & Rhin., A. M. A., 1931, p. 100.

The changes occurring in the blood during infection have been well summarized by Weiss [7] in describing the "staff count," or the number of neutrophils with nonsegmented nuclei. During a mild infection there is an increase in the number of leukocytes and neutrophils, chiefly of the type with segmented nuclei. In a severe infection also both leukocytosis and neutrophilia occur, but a large proportion of the latter forms are represented by cells with nonsegmented nuclei. An overwhelming infection is characterized by a relatively low leukocyte count, a variable percentage of neutrophils and a marked increase in neutrophils with nonsegmented nuclei and evident toxic changes. The latter observation has been emphasized recently by Kugel and Rosenthal,[8] who used the term degenerative index to express the ratio of the number of neutrophils with toxic changes to the total number of neutrophils. The gravity of the prognosis is in direct proportion to the preponderance of the former cells over the latter. Accompanying the changes in the total leukocyte count and in the number of neutrophils, the eosinophils disappear from the circulation, and a concomitant fall in monocytes and lymphocytes takes place.

The reparative stage of a mild or severe infection is evidenced by a fall in the total number of leukocytes and neutrophils, a transitory rise in the number of monocytes and the reappearance of eosinophils. The final stage is marked by a short period of predominance of lymphocytes, the number ranging from 50 to 60 per cent of the total number of leukocytes. Weiss concluded that the peak of the staff count coincides with the height of infection and that the count falls when the infection is being overcome. A persistently high staff count indicates the continuance of infection or the presence of a complication. The information to be obtained from repeated staff counts, he believed, is more reliable than that from the total leukocyte count or from the number of neutrophils present in the differential count.

Because of the ease with which a filamented cell count or staff count may be made and the paucity of articles dealing with its application in the pediatric literature, it seemed advisable to check the value of this procedure by comparison with the total leukocyte and differential counts as ordinarily applied to the diagnosis of an acute infection. Cases of appendicitis were chosen for study, since the preoperative leukocyte, differential and filamented cell counts could be checked by the pathologic observations in the cases in which operation was performed.

7. Weiss, Arthur: The Staff Count: Its Importance in Acute Infectious Disease, Arch. Int. Med. **48**:399 (Sept.) 1931.

8. Kugel, M. A., and Rosenthal, Nathan: Pathologic Changes Occurring in Polymorphonuclear Leukocytes During the Progress of Infections, Am. J. M. Sc. **183**:657 (May) 1932.

CASES INCLUDED IN STUDY

A series of 41 cases of appendicitis encountered at the clinic was divided into four groups: cases of (1) acute purulent appendicitis, (2) subacute catarrhal appendicitis, (3) chronic catarrhal appendicitis and (4) clinical appendicitis in which operation was not performed.

Acute Purulent Appendicitis.—This group consisted of 26 cases in which acute or subacute purulent appendicitis was proved by pathologic examination; it included

TABLE 1.—*Data from Blood Counts on Children with Acute Purulent Appendicitis*

Case	Age, Years	Sex	Leukocyte Count Before Operation	Polymorphonuclear Neutrophils, Percentage	Ratio of Nonfilamented to Filamented Cells
1	2	M	38,000	71	50:21
2	3	F	19,600	68	35:33
3	3	M	17,500	89	56:33
4	4	F	19,000	87	61:26
5	5	M	24,100	87	50:37
6	5	F	18,900	78	50:28
7	6	F	10,300	79	35:44
8	7	M	19,200	74	64:10
9	8	F	11,700	77	71:6
10	8	M	15,800	78	52:26
11	8	M	17,400	82	35:47
12	8	M	12,600	76	40:36
13	9	M	16,600	80	16:64
14	9	M	14,000	83	40:43
15	9	F	6,500	88	60:28
16	10	F	18,100	91	73:18
17	11	F	32,300	92	63:29
18	12	M	15,000	79	27:52
19	12	M	14,000	80	42:38
20	13	M	17,000	85	79:6
21	13	F	15,000	90	35:55
22	13	M	16,500	87	16:71
23	13	M	12,100	79	27:52
24	14	F	16,700	86	23:63
25	14	F	13,500	88	73:15
26	14	F	12,800	69	15:54

TABLE 2.—*Data from Blood Counts on Children with Subacute Catarrhal Appendicitis*

Case	Age, Years	Sex	Leukocyte Count Before Operation	Polymorphonuclear Neutrophils, Percentage	Ratio of Nonfilamented to Filamented Cells
1	3	M	12,000	80	70:10
2	6	M	7,600	82	61:21
3	12	F	6,100	68	28:40
4	13	F	7,800	47	21:26
5	13	F	12,800	90	37:53
6	14	M	9,000	50	15:35

the cases in which gangrene was present or rupture had occurred (table 1). The pathologic changes in these cases were marked neutrophilic infiltration, purulent exudate on the surface of the appendix, edema, congestion of the vessels and, in some instances, perforation of the appendix and peritonitis.

Subacute Catarrhal Appendicitis.—This group consisted of 6 cases in which the condition was diagnosed by the pathologist as subacute catarrhal appendicitis. In these cases there was a moderate degree of inflammation of the appendix with slight neutrophilic infiltration of the walls, edema and congestion (table 2).

Chronic Catarrhal Appendicitis.—This group was composed of 4 cases of chronic catarrhal appendicitis, in which the appendix was devoid of neutrophilic invasion and the lymphoid structure of the wall was preserved (table 3). The clinical diagnosis of appendicitis was not supported by the results of the pathologic examination in these cases.

Clinical Appendicitis; Operation Not Performed.—This group contained 5 cases in which the patient was not operated on but appendicitis was suspected because of the history or the physical signs (table 4). In 1 case gastro-intestinal disturbance proved to be the source of the symptoms. In another the presence of scarlet fever and clinically acute appendicitis made immediate operative intervention inadvisable; on subsidence of symptoms, however, surgical treatment was postponed indefinitely.

TABLE 3.—*Data from Blood Counts on Children with Chronic Catarrhal Appendicitis*

Case	Age, Years	Sex	Leukocyte Count Before Operation	Polymorphonuclear Neutrophils, Percentage	Ratio of Nonfilamented to Filamented Cells
1	7	F	9,000	71	23:48
2	7	M	7,900	73	65:8
3	10	F	6,600	62	22:40
4	7	M	9,300	68	23:45

TABLE 4.—*Data from Blood Counts on Children with Clinical Appendicitis Not Operated On*

Case	Age, Years	Sex	Leukocyte Count Before Operation	Polymorphonuclear Neutrophils, Percentage	Ratio of Nonfilamented to Filamented Cells
1*	4	M	17,000	67	49:18
2	5	M	6,600	64	35:29
3	12	F	6,500	82	49:33
4	13	M	9,200	45	17:28
5†	13	F	14,100	78	66:12

* This patient had acute gastro-enteritis.
† This patient had scarlet fever and acute appendicitis.

BLOOD COUNT IN CASES OF APPENDICITIS

Total Leukocyte Count.—There is usually definite leukocytosis in cases of appendicitis of all degrees of severity, although this is not invariable. Müller,[9] in a study of 640 cases of acute appendicitis observed during the period from 1924 to 1929, found that in 52, or 8.1 per cent, there was no elevation of the leukocyte count, and he ascribed this observation to the position of the appendix, which was such that the peritoneum was not involved by an extension of infection.

When dealing with appendicitis in children, it must be remembered that the leukocytes increase rapidly and to a marked degree during infection. The normal values for adults do not hold in early child-

9. Müller, Ludwig: Ueber die Ursachen fehlender oder relativ geringer Leukozytose bei akuter Appendizitis, Beitr. z. klin. Chir. **155**:467, 1932.

hood, and allowance must be made for this factor. Most authorities agree that a leukocyte count of more than 10,000 per cubic millimeter of blood indicates a significant increase at any age, unless it is in the first two years of life, when the total leukocyte count may normally approximate this value. The degree of leukocytosis has been taken as an index of the patient's resistance to the infection.

In the first group the leukocyte count was higher than 10,000 per cubic millimeter in all but 1 case. The highest count was 38,000, and it was found in the case of the youngest patient, a child aged 2 years. The highest counts predominated in the lowest age group, and the usual preoperative leukocyte values were from 15,000 to 18,000 per cubic millimeter.

In the second group the total leukocyte count was higher than 10,000 per cubic millimeter in 2 cases only. In the other cases the leukocyte count could be considered normal since it varied between 6,000 and 9,000 per cubic millimeter.

In the third group all the leukocyte counts were less than 10,000 per cubic millimeter and were normal values for the ages represented.

In the fourth group half the patients had normal leukocyte counts. In 1 case which proved to be one of infection of the bowel, the count was 17,000 per cubic millimeter; in another, in which scarlet fever was complicated by acute appendicitis, the count was 14,100 per cubic millimeter.

The presence of an increased leukocyte count concurred with the diagnosis of acute appendicitis made by the pathologist in 96 per cent of the cases in the first group, whereas in the cases of subacute appendicitis leukocytosis was an inconstant feature and in the chronic form it was absent. The presence and degree of leukocytosis bear a direct relation to the severity of the inflammation in cases of appendicitis among children, and when present are valuable diagnostic aids.

Neutrophil Count.—The leukocytosis which occurs in an acute infection is due to the relative increase in the number of polymorphonuclear neutrophils in the circulating blood. The degree of increase of these cells has been regarded as an index of the severity of the infection and varies in direct relation to it. This being true, it is of much assistance to compare the degree of leukocytosis with the increase in neutrophils as an expression of the resistance of the patient on the one hand, and of the severity of the infection on the other. As in the case of the total leukocyte count, one must be cognizant of the variation in the percentage of neutrophils due to age. Talbot,[10]

10. Talbot, F. B.: The Blood and Blood Diseases of Infancy and Childhood, in Nelson Loose Leaf Medicine, New York, Thomas Nelson & Sons, 1920, vol. 4, p. 60.

from a review of the blood in childhood, stated that 34 per cent of neutrophils is an average value for children in the first year of life, 50 per cent, for those from 6 to 8 years old, and 58 per cent, for those 10 years old, and that a gradual rise to the level in the adult takes place at from 12 to 14 years of age. One must not overlook the fact that a percentage of neutrophils that would be normal for an adult represents an increase for children less than 5 years of age.

In the first group there was a significant increase of neutrophils at all ages, the proportion varying from 68 per cent for a child aged 3 years to 92 per cent for a girl aged 11 years. The average number for this group was 85 per cent.

In one-half the cases in the second group there was no increase of neutrophils; in 2 cases the percentage of these cells was reduced. The highest value in this group was 90 per cent, and it was increased out of proportion to the pathologic changes and the slight increase in the total leukocyte count of 12,800 per cubic millimeter.

In the third group there was a slight increase in the neutrophil count in all cases, 73 per cent being the highest value. All the percentages were higher than the three lowest values in the preceding group and ranged constantly between 62 and 73 per cent, which may be considered as being the upper limit of the normal count.

In 2 of the 5 cases in the fourth group the percentage of neutrophils was increased, although only to a moderate degree, and this increase occurred in only 1 of the cases in which a high leukocyte count also was present. Except in the first group of acute cases, the increase in neutrophils was not marked. The degree of increase in these cells paralleled closely the severity of the infection but with decreasing accuracy in the subacute or chronic cases.

Filamented Cell Counts.—A count of the filamented and nonfilamented forms of neutrophils was made at the same time that the usual differential count was made on 200 cells. The counts of filamented and nonfilamented cells are expressed as percentages of the total leukocyte count. For example, a nonfilamented cell count of 30 means that nonfilamented forms of neutrophils constitute 30 per cent of the total leukocyte count. A filamented cell count of 40 means that 40 per cent of the total number of leukocytes are filamented neutrophils. The sum of the two values, 30 and 40 per cent or 70 per cent, represents the total percentage of neutrophils in the leukocyte count.

The ratio of nonfilamented to filamented neutrophils is normally less than 1. In cases in which there is marked increase of nonfilamented forms, the ratio approaches or becomes greater than 1. A high nonfilamented-filamented cell ratio, indicating a predominance of neutrophils with nonfilamented nuclei over those with filamented nuclei, has the same significance as the so-called "left shift" of the poly-

morphonuclear neutrophils, which also indicates an increased proportion of nonfilamented cells.

In dealing with abnormal values for nonfilamented and filamented neutrophils, one must have some basis for guidance in regard to normal values. The upper limit of the normal value for the nonfilamented forms in the total leukocyte count has been established as 16 per cent by Farley, St. Clair and Reisinger, on the basis of a study of the blood smears of 100 normal, healthy adults. As no similar value has been given for children to my knowledge, my associates at the clinic and I determined the normal value in 30 children free from infection; this value was established by the history, results of physical examination and normal leukocyte count and the presence of a neutrophil count of less than 70 per cent of the total leukocyte count. Allowance was made for the lower values for neutrophils that are normal in the age group from 1 to 5 years. To obtain a better idea of the number of filamented neutrophils at the various ages of infancy and childhood, nonfilamented and filamented cell counts were made on the blood smears of 2 patients for each year of age from 1 to 15. In only 6 of the 30 subjects did the number of nonfilamented neutrophils constitute more than 20 per cent of the total leukocyte count. The range of nonfilamented forms for the whole group of children was from 5 to 29 per cent of the total leukocyte count, with the median value 15 per cent. In only 3 instances was the nonfilamented-filamented cell ratio greater than 1, and in only 1 case was the difference in number in favor of the nonfilamented neutrophils by more than 2 cells. A nonfilamented cell count in excess of 30 appears to be beyond the upper limit of the normal value for childhood, regardless of the age of the child.

In all but 6 of the cases of acute appendicitis in the first group the nonfilamented cell count exceeded 30. In each of these 6 cases leukocytosis was present, and an increase in the percentage of neutrophils took place, indicating the presence of acute infection. Three of the 6 patients with nonfilamented cell counts of less than 30 were reported by the pathologist to have gangrenous appendixes. When the ratio of nonfilamented to filamented neutrophils was considered, the discrepancy was even greater. In 16 cases in this group, the ratio exceeded 1, whereas in 10 cases the ratio was less than 1. The failure of the nonfilamented forms to increase in proportion to the increase in total leukocytes and polymorphonuclear neutrophils is evident in several cases. However, in cases in which the percentage of neutrophils was higher, there was also a greater proportion of nonfilamented forms, indicating a greater demand for these phagocytes in the presence of acute infection. It may be true that a low nonfilamented cell count or a low nonfilamented-filamented cell ratio indicates good resistance

on the part of the patient. An increase in the nonfilamented forms as the expression of a greater demand for neutrophils in combating the infection would not be expected in such a case.

In the second group only one-half the patients had a nonfilamented cell count in excess of 30, and in only 2 cases was the ratio greater than 1. In all other cases the nonfilamented-filamented cell ratio was definitely less than 1. There was 1 notable exception in this group, a case in which there was an elevation of the leukocyte count, a percentage of neutrophils of 90 and a ratio of nonfilamented to filamented forms of 37:53 with a pathologic diagnosis of subacute appendicitis. The lower incidence of elevated nonfilamented cell counts is to be expected, since the degree of infection in the appendix was shown to be only slight or moderate.

In the third group 3 of the 4 patients had low nonfilamented cell counts (less than 30). The fourth patient had a ratio of 65:8, and no cause was found for such a high proportion of nonfilamented neutrophils. The total leukocyte and neutrophil counts in this case were within the normal range.

Of the 5 patients in the fourth group who were not operated on, 4 had nonfilamented cell counts of more than 30. There was a marked increase of nonfilamented cells in the case of gastro-enteritis and in that of scarlet fever and appendicitis (table 4).

It may be said that in cases of appendicitis in children the nonfilamented cell count tends to parallel the total neutrophil count as an index of the severity of the infection. In cases in which there are moderate or mild degrees of appendical infection, the increase in the nonfilamented neutrophils is variable and less reliable. This applies also to the ratio of nonfilamented to filamented cells.

Comparison of Diagnostic Values of the Total Leukocyte Count, Neutrophil Count and Nonfilamented-Filamented Cell Ratio.—The nonfilamented cell count is of greater diagnostic aid in cases of acute appendicitis than in those of subacute or chronic appendicitis, as shown by comparison with the total leukocyte and neutrophil counts and with the pathologic observations. The degree of preponderance of the nonfilamented neutrophils over the filamented forms in cases of acute appendicitis may give a hint of the severity of the infection, even in cases in which the leukocyte count and neutrophil values are not elevated. Normal or low values for leukocytes and neutrophils are occasionally found in instances of overwhelming infection. In a recent article, Rogatz [11] stated that the increase of staff cells or nonsegmented neutrophils determined by the Schilling count was a more reliable

11. Rogatz, J. L.: The Schilling Blood Count as an Aid in the Diagnosis of Acute Appendicitis in Children, J. Pediat. **4**:757 (June) 1934.

indicator of the presence of acute appendicitis in children than the total leukocyte count. He stated that a normal percentage of staff cells indicates absence of acute inflammation regardless of the leukocyte count. Experience at this clinic does not bear out such a view, and in the diagnosis of appendicitis of all grades the preferred order of reliability is: (1) the total leukocyte count, (2) the increase in neutrophils and (3) an increase in nonfilamented neutrophils with a nonfilamented-filamented cell ratio exceeding 1.

Prognostic Significance of the Hemogram.—In each of the 3 fatal cases in the series, there was marked preponderance of nonfilamented over filamented neutrophils (61:26, 64:10 and 71:6). One patient with a ratio of 79:6 on admission and a diagnosis of ruptured appendix

TABLE 5.—*Data in Case 1*

Date	Leukocyte Count	Polymorphonuclear Neutrophils, Percentage	Ratio of Nonfilamented to Filamented Cells	Lymphocytes, Percentage	Monocytes, Percentage	Eosinophils, Percentage	Basophils, Percentage	Comment
9/18/33 (a.m.)	19,000	74	52:22	12	13.5	0.5	..	Pain in lower left quadrant; nausea
(p.m.)	15,000	84	52:32	5	15	None	..	Vomiting twice; appendectomy performed
9/19/33	14,400	79	51:28	15	6	None	..	
9/21/33	12,100	71	48:23	..	...	1	..	
9/23/33	15,300	65	51:14	28	4	3	..	Temperature normal
9/28/33	13,500	72	21:51	19	6	3	..	
10/ 2/33	10,300	60	14:46	30	8	1	1	Patient dismissed

with generalized peritonitis survived. I agree with Mullin and Large that an increase in nonfilamented neutrophils to a value of more than 50 per cent of the total differential leukocyte count demands a guarded prognosis. In the 10 cases of the group in which there was a nonfilamented neutrophil count in excess of 50, 3 of the patients died.

The value of the nonfilamented cell count in prognosis is perhaps its most useful application. An increasing nonfilamented cell count is an unfavorable sign, whereas an increase in the filamented forms is the usual accompaniment of a favorable convalescence. Two cases illustrative of the prognostic value of the nonfilamented cell count are included here. The behavior of the filamented and nonfilamented cells may be noted in tables 5 and 6.

REPORT OF CASES

CASE 1.—A boy, aged 13 years, complained of diffuse abdominal pain and nausea on Sept. 15, 1933, three days before he was seen by a physician. He took

a laxative the day after the pain began. The examining physician found tenderness and rigidity in the left lower abdominal quadrant extending to the median line. On rectal examination tenderness was found to be more marked on the left side. The temperature recorded by mouth was 100.4 F., and the pulse rate was 86 per minute. The boy vomited greenish material during the examination. A preoperative diagnosis of acute appendicitis was made, and immediate operation was advised.

At operation the appendix was seen to be acutely inflamed. The tip of the organ pointed toward the left, and a small perforation was noted in the gangrenous portion of this tip, which undoubtedly accounted for the symptoms on the left side. The appendix was removed and one rubber drain was inserted. The temperature fell to a normal level and remained so after the fifth postoperative day. The gradual fall in the total leukocyte count and in the percentage of neutrophils may be noted in table 5. The final nonfilamented cell count of 14 was indicative of the favorable convalescence in this case. The boy was dismissed on the fourteenth day after operation.

TABLE 6.—*Data in Case 2*

Date	Leukocyte Count	Polymorphonuclear Neutrophils, Percentage	Ratio of Nonfilamented to Filamented Cells	Lymphocytes, Percentage	Monocytes, Percentage	Eosinophils, Percentage	Basophils, Percentage	Comment
1/23/34	19,200	79	64:15	10	11	..	..	
1/24/34	17,500	83	64:19	12	5	..	..	Operation
1/25/34	18,600	77	60:17	15	8	..	..	
1/27/34	18,900	85	67:18	12	2	1	..	
1/29/34	18,000	80	69:11	17	3	..	..	Wound draining
2/ 1/34	11,500	75	57:18	19	5	..	..	
2/ 3/34	10,300	65	46:19	32	3	..	..	Convalescence good
2/ 5/34	16,100	66	31:35	32	2	..	..	
2/ 8/34	12,800	64	40:24	35	6	1	..	
2/10/34	13,700	55	32:23	..	..	..	..	
2/16/34	14,500	76	65:11	18	6	..	..	Temperature rising; pneumonia in base of right lung
2/22/34	21,900	93	74:19	4	3	..	..	Further extension of pneumonia
2/23/34	25,500	92	78:14	7	1	..	..	Tapping for relief of empyema
2/26/34	57,200	93	83:10	6	..	..	..	Second pleurocentesis
2/27/34	.....	..	.....	..	..	..	..	Temperature 108 F.; death

CASE 2.—A boy, aged 7 years, had generalized abdominal pain one week before his admission to the hospital. The pain became localized in the right side of the abdomen the day after its onset. The patient vomited twice and had a temperature of 102 F. or more daily for six days. Rigidity of the abdomen was noted by the physician at the patient's home six days before admission. The boy had taken liquid petrolatum and several enemas to relieve constipation after the onset of the abdominal symptoms. He was admitted to the hospital on Jan. 23, 1934. Examination at that time disclosed tenderness and rigidity of grade 3 of the right rectus muscle and the presence of a palpable mass in the right lower quadrant of the abdomen. The temperature was 102 F., and the pulse rate was 120 a minute. A diagnosis of appendicitis with rupture and formation of an abscess was made.

The following day the appendical abscess was drained through a high right rectus incision. The abscess was seen to be retrocecal and to lie just beneath the liver. The appendix was removed. The differential blood count after operation may be noted in table 6. Except on the day after operation the boy had a tem-

perature of less than 101 F., and drainage from the wound was free. Until February 13 a favorable outcome seemed likely, as indicated by the falling leukocyte count and the decrease in the number of polymorphonuclear neutrophils and nonfilamented forms. On that day the temperature began to rise, and there was an increase in the number of leukocytes, polymorphonuclear neutrophils and nonfilamented forms, which indicated the presence of a complication. There were signs of pneumonia at the base of the right lung, but in order to rule out the presence of a subphrenic abscess exploration of the operative region was made; no abscess was encountered. The boy received a transfusion of blood three days later, and on the following day pleurocentesis was done because of signs of fluid at the base of the right lung; 200 cc. of purulent fluid was removed. This procedure was repeated two days later, and the boy was given a transfusion again the following day. His temperature indicated a septic condition at this time, and he gradually became exhausted and died on February 27. A week before the patient's death the number of leukocytes, neutrophils and nonfilamented cells rose to high levels and indicated clearly the unfavorable prognosis.

SUMMARY AND CONCLUSIONS

From an analysis of 41 cases of appendicitis among children, I would place in order of their reliability as aids in diagnosis (1) an increase in the total leukocyte count, (2) an increase in the number of neutrophils and (3) an increase in the number of nonfilamented neutrophils with a nonfilamented-filamented cell ratio exceeding 1.

Certain points in regard to the filamented-nonfilamented cell count seem worthy of mention. In modifications of the well established Schilling count, it has been simplified to the point of eliminating consideration of toxic changes in the neutrophils, which are often of greater significance than the number of nonfilamented neutrophils. The presence of these toxic changes in the neutrophils is of definite prognostic import.

The presence of very immature leukocytes in the course of a case of appendicitis is important evidence of the demand being made on the bone marrow. Immaturity in the leukocytes extending as far as the promyelocyte stage is sometimes seen in cases of acute appendicitis. The nonfilamented cell count provides no means of showing how immature the nonfilamented forms may be.

The nonfilamented cell count may increase in advance of the rise in total leukocytes or neutrophils. An increase in any or all of these forms should warn one of the possibility of extension of the infection.

The prognostic value of the nonfilamented cell count is perhaps its greatest usefulness. In acute appendicitis, an initial high nonfilamented cell count means that the outlook is bad. With the total percentage of neutrophils higher than 90 and with less than 10 per cent of these filamented forms, the prognosis is grave. A falling nonfilamented cell count, or a nonfilamented-filamented cell ratio of less than 1 is a good

sign, as are also the reappearance of eosinophils and monocytes and the disappearance of neutrophils of toxic type from the peripheral circulation.

The nonfilamented cell count is of value in the diagnosis of appendicitis, since it parallels the neutrophil count during the course of the infection. When considered with the total leukocyte count and the percentage of neutrophils the nonfilamented cell count is an important diagnostic aid, but it is not reliable alone in a sufficient number of cases to be of the same diagnostic worth as the total leukocyte count and the percentage of neutrophils.

ABSORPTION OF UNDIGESTED PROTEINS IN HUMAN BEINGS

IV. ABSORPTION OF UNALTERED EGG PROTEIN IN INFANTS AND IN CHILDREN

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It has been shown in previous communications [1] that following the ingestion of such proteins as those of fish and eggs, detectable amounts of these substances are absorbed into the circulation in most normal adults. Absorption from the rectum was also demonstrated by the same technic.[1c] The present communication deals with an investigation of these phenomena of absorption in infants and children.

Egg was chosen as the protein most suitable for study because it is a common constituent of the diet of the average child and is easily administered. The technic employed in this investigation was practically the same as that reported in the previous communications. A brief summary follows:

METHODS OF INVESTIGATION

Egg in any form was excluded from the diet of the subject on the day that passive local sensitization was induced. This procedure consisted of an intracutaneous injection into the flexor surface of the forearm of about 0.05 cc. of a special serum obtained from a person who was sensitive to eggs (K 4 serum). On the following morning the test meal, containing egg, was taken by the fasting subject. No attempt was made to clear the intestinal tract before the test. Following the meal, the sensitized cutaneous site was kept under observation. The appearance of erythema or a wheal marked the onset of the local reaction, which indicated that unaltered egg protein had entered the circulation.

The K 4 serum used for producing passive local sensitization was the same as that employed in the series of adults. It was obtained from a patient 2½ years of age, suffering from eczema, asthma and urticaria, who was extremely sensitive

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From the Jewish Hospital.

Read before the Brooklyn Pediatric Society, Oct. 17, 1929.

1. (*a*) Walzer, M.: Studies in Absorption of Undigested Proteins in Human Beings: I. A Simple Direct Method of Studying the Absorption of Undigested Proteins, J. Immunol. **16**:143 (Sept.) 1927. (*b*) Brunner, M., and Walzer, M.: Absorption of Undigested Proteins in Human Beings: The Absorption of Unaltered Fish Proteins in Adults, Arch. Int. Med. **42**:172 (Aug.) 1928. (*c*) Sussman, H.; Davidson, A., and Walzer, M.: Absorption of Undigested Proteins in Human Beings: III. The Absorption of Unaltered Egg Protein in Adults, ibid. **42**:409 (Sept.) 1928.

to eggs. (The history of this case has been set forth in detail in an earlier communication.[1a]) The serum was used either in a dilution of 1:10 or in undiluted form.

The test meal consisted of the white of one egg mixed with milk and flavored with sugar and cocoa. Water was occasionally substituted for milk as the diluent. The total volume of the drink measured 2 ounces (59 cc.) or less. In this study, as well as in that on adults, slight variations in the total volume of the test meal did not seem to influence the results obtained. In most instances the meal was taken willingly, but occasionally it was necessary to force it on the subject. Egg yolk was excluded from the test meal as no antibodies for this antigen were present in the K 4 serum.

The reaction at the sensitized site which marked the time of entry of the egg protein into the blood stream usually started as a slight blush, accompanied by pruritus. The erythema then increased rather rapidly in extent and intensity, and at its center one or several small wheals appeared. In the more marked reactions the wheals increased in size until they coalesced to form one large, round or irregular central wheal. The reaction was considered positive even when the erythema appeared without the wheal or vice versa. Pruritus alone without erythema or wheal was not considered a positive reaction. (A detailed description of the entire cutaneous reaction was presented in another communication.[2]) The interval between the beginning of the test meal and the first objective sign of the cutaneous reaction was considered the absorption or reaction time of the subject. The sensitized site was kept under observation for at least two hours after the test meal.

In certain instances in which the reaction failed to appear, the sites were subsequently tested directly by an intracutaneous injection of egg extract to determine whether passive local sensitization had been effected. A positive cutaneous reaction was almost always obtained. In this study, as in those previously reported,[1a, b] failure of the skin to accept passive local sensitization did not seem to be an important factor in the explanation of the negative results obtained.

The present investigation consisted of studies on three groups of subjects. The first was made up of eighteen hospital patients, for whom the experimental methods were varied somewhat in order to determine the technic which would be most satisfactory for use with children. The second group consisted of fifty normal children in an orphanage. The technic employed was uniform throughout this series. In the third group were four infants less than 1 week old. The three studies were made in January, October and November of the same year (1926).

Thirty tests were made on the eighteen subjects included in the hospital series. The results in only twelve cases are presented in table 1, representing the tests in which a relatively uniform technic was employed. A 1:10 dilution of K 4 serum was used for sensitization in all the cases. The ages of the subjects varied from 1 to 10 years. There were ten boys and two girls in the series. The patients had been hospitalized because of an acute or chronic illness, such as pneumonia, endocarditis, arthritis, anemia or syphilis (table 1). All the subjects, however, were free from obvious gastro-intestinal disturbances. In cases 3 and 6 the rectal temperature was 100 F. at the time of testing. In all other instances there was no fever.

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2. Walzer, A., and Walzer, M.: Urticaria: II. The Experimental Wheal Produced on Normal Skin Through Internal Channels, Arch. Dermat. & Syph. **17**:659 (May) 1928.

Of the twelve subjects tested with a uniform technic the absorption of unaltered protein was demonstrated in ten, or 83 per cent. The absorption or reaction time varied from twenty-five to one hundred and five minutes. The average reaction time for this group was fifty-eight minutes.

In the second series of tests on fifty normal children at an orphanage, the subjects ranged in age from 11 months to 4 years. There were twenty-seven girls and twenty-three boys in the group. K 4 serum was used in this study as in the preceding one. In view of the fact that the serum had aged and lost some of its activity, each subject was sensitized with undiluted serum as well as with a serum of a 1:10 dilution. For the sake of economy only 0.025 cc. of serum was injected in each site. The test meal administered on the following morning consisted of the white of one egg, 1 ounce (29.6 cc.) of milk, ½ teaspoonful of cocoa and ½ teaspoonful of sugar. The sensitized site was kept under observation for at least three hours following the test meal. The data obtained on these subjects are presented in table 2 and summarized in table 3.

TABLE 1.—*Absorption of Unaltered Egg Proteins in Hospitalized Children* *

Case	Date	Age, Years	Sex	Diagnosis	Reaction Time, Minutes
1	1/29/26	10	F	Endocarditis	25
2	1/21/26	3	F	Bronchopneumonia	105
3	1/26/26	2¾	M	Syphilis	50
4	1/18/26	1	M	Bronchopneumonia	60
5	1/18/26	8½	F	Rheumatic arthritis	60
6	1/27/26	3	M	Cerebrospinal syphilis	0
7	1/24/26	3	M	Secondary anemia	75
8	1/24/26	1	M	Bronchopneumonia	60
9	1/24/26	1½	M	Bronchopneumonia	60
10	1/24/26	6	M	Chronic pulmonary infection	0
11	1/30/26	6	M	Secondary anemia	45
12	1/30/26	2	M	Bronchopneumonia	45

* Sensitization was produced with 0.05 cc. of K 4 egg serum in a dilution of 1:10. The test meal consisted of the white of one egg in milk.

Of the fifty subjects tested, twenty-four (48 per cent) manifested a positive reaction at the site sensitized with the 1:10 dilution of serum, and thirty-five (70 per cent) reacted with the undiluted serum. All subjects reacting with the diluted serum gave positive reactions with the undiluted serum. In this series the reaction time varied from twenty-seven to ninety-five minutes with the diluted serum, the average time being about sixty-two minutes. With the undiluted serum the reaction time varied from twenty-five to ninety-five minutes, the average time being fifty-six minutes. The shortening of the average reaction time with the greater concentration of the serum confirms a similar finding in the series of adults. The reaction time in only five cases was thirty minutes or less. In no instance was the time shorter than twenty-five minutes. It exceeded ninety minutes in only two tests. Hence, with only two exceptions, the absorption phenomenon occurred within from twenty-five to ninety minutes after the test meal or not at all.

A comparison of the results obtained in the first two groups of cases discloses a higher percentage of reactions in the hospital series. As the K 4 serum had aged and had therefore deteriorated to some extent in the nine month interval between the two studies, the smaller percentage obtained in the later series was to be expected.

The combined results obtained in the first two series, totaling sixty-two children, show that in forty-five (75.5 per cent) of the subjects the reaction at the sensitized sites was positive, thus demonstrating that unaltered egg protein was absorbed into the circulation following its ingestion (table 3).

TABLE 2.—*Absorption of Unaltered Egg Protein in Fifty Normal Orphans* *

Case	Age, Months	Sex	Reaction Time, Minutes: Undiluted Serum	Reaction Time, Minutes: Dilution 1:10	Case	Age, Months	Sex	Reaction Time, Minutes: Undiluted Serum	Reaction Time, Minutes: Dilution 1:10
1	27	F	58	0	26	35	F	55	0
2	28	M	35	40	27	32	F	53	58
3	18	F	77	+§	28	38	F	0	0
4	26	F	30	35	29	42	F	45	55
5	18	M	0	0	30	32	F	0	0
6	28	M	0	0	31	23	M	0	0
7	24	M	+§	0	32	40	F	30	81
8	27	M	0	0	33	36	M	0	0
9	18	M	80	0	34	40	F	49	77
10	20	M	0	0	35	42	F	59	0
11	13	M	0	0	36	43	F	45	47
12	14	F	0	0	37	38	F	55	0
13	19	M	71	95	38	40	F	65	75
14	20	M	95	0	39	48	F	95	0
15	11	F	45	95	40	36	M	0	0
16	18	F	25	45	41	44	F	42	72
17	31	F	0	0	42	38	F	0	0
18	42	F	90	0	43	42	M	48	50
19	38	F	58	90	44	38	F	70	70
20	36	F	0	0	45	30	F	40	0
21	26	F	83	0	46	42	M	42	70
22	40	M	40	61	47	31	M	0	0
23	32	M	27	27	48	35	M	80	+§
24	34	M	72	+§	49	42	M	45	52
25	32	M	35	37	50	43	M	52	75

* Sensitization was produced with 0.025 cc. of K 4 egg serum. The test meal consisted of one egg, 1 ounce of milk, ½ teaspoonful of sugar and ½ teaspoonful of cocoa.
§ A positive reaction, in which the reaction time was not noted, is indicated.

TABLE 3.—*Summary of Results Obtained in All Subjects*

Series	1	2		3		Totals
Type of subjects	Hospitalized children	Normal Orphans		New-born Infants		
Age limit	1-10 yrs.	1-4 yrs.		4-7 days		
Serum employed	K 4	K 4		K 6		
Dilution of serum	1:10	1:10	Undiluted	1:10	Undiluted	
Number of subjects	12	50*	50*	2	2	66
Number of positive reactions	10	24	35	2	2	49
Positive reactions, per cent	83.3	48	70	100	100	74.2
Reaction time, minutes	25-105	27-95	25-95		55	
Average reaction time, minutes	58	62	56			

* Each patient was tested with diluted and undiluted serum.

A small series of new-born infants was then studied to see whether the absorption phenomenon could be demonstrated at this early age. For this purpose two infants, R. and M., aged 3 and 4 days, respectively, were sensitized with fresh serum (K 6) secured from the same patient from whom the K 4 serum had been obtained. Sensitization was effected by an intracutaneous injection of about 0.55 cc. of a 1:10 dilution of serum. As the infants were breast fed, eggs were

excluded from the diet of the mothers during the period of the experiment. Following the regular feeding at 9:30 p. m. on the day on which they were sensitized, the infants were given only water at 12:45 a. m. At 2:45 a. m. they received 1 drachm (1.77 Gm.) of egg white in 2 ounces (59 cc.) of water. M. finished this test meal at 3 a. m. and R. at 3:15 a. m. The reactions developed strongly in each child between 3:15 and 3:30 a. m.

In another experiment two infants, P. K. and P. L., aged 6 and 7 days, respectively, were sensitized with 0.05 cc. of undiluted K 6 serum. The following morning they received their regular feedings. At 11:45 a. m. when the regular feeding was due, P. K. received ½ drachm (0.89 Gm.) of egg white in 2 ounces (59.2 cc.) of formula. He finished this meal at 12:15. The reaction appeared at 12:40 p. m., fifty-five minutes after the beginning of the test meal. P. L. received a similar test meal at 11:45 a. m. and finished it at 12:25 p. m. The reaction in this case also appeared at 12:40 p. m.

It was difficult to establish the exact reaction time in the infants, as it took them from fifteen to forty minutes to consume the test meal. In every instance, however, the reaction appeared within fifty-five minutes after the beginning of the test meal.

COMMENT

An analysis of the results of the tests in sixty-six infants and children, varying in age from 3 days to 10 years of age, reveals that forty-nine, constituting 74.2 per cent of the total number, manifested the absorption phenomenon. On the basis of arguments set forth in a previous communication,[1a] this may be interpreted to indicate that in the usual normal infant unaltered food substances are constantly passing into the circulation.

Anderson, Schloss and Meyers[3] showed in an earlier study that precipitins for milk, egg and other proteins appeared in the blood of normal infants following the initial inclusion of these foods in the diet. These antibodies persisted only temporarily and disappeared in a few weeks. In marasmic babies, they usually occurred in larger amounts and remained for a longer period of time than in normal infants.

Our own observations in this and previous studies indicated that the absorption of unaltered protein is not a temporary or unusual occurrence but is a normal phenomenon, taking place at all ages from birth throughout life.

The incidence (74.2 per cent) of the absorption phenomenon, as demonstrated in the present investigation in infants and children, compares favorably with the results obtained in the adult series (85.3 per cent) which were reported in a previous study. The results obtained in the two series, however, cannot be directly compared, as experimental conditions varied somewhat in the two studies.

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3. Anderson, A.; Schloss, O. M., and Meyers, E.: Intestinal Absorption of Antigenic Proteins by Normal Infant, Proc. Soc. Exper. Biol. & Med. **23**:180, 1925.

CONCLUSIONS

1. The absorption into the circulation of unaltered egg protein from the digestive tract was demonstrated in forty-five of sixty-two children (72.5 per cent), varying from 11 months to 4 years of age. It also was demonstrated in each of four infants less than 1 week old.

2. The absorption time of these subjects varied from twenty-five to one hundred and five minutes. By far the greater number reacted between forty-five and seventy-five minutes after the ingestion of the egg meal.

3. The absorption of unaltered egg protein is a normal and physiologic phenomenon in infants and children as in adults.

ADDENDUM: This paper is presented as it was read on Oct. 17, 1929, before the Brooklyn Pediatric Society. Certain unavoidable circumstances prevented the earlier publication of the work, but we have repeatedly stated our conclusions in other writings.[4] Since this paper appears in its original form, the investigations of other workers on the same subject which have appeared since that time[5] are not reviewed.

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4. Walzer, M.: Asthma and Hay Fever, Springfield, Ill., Charles C. Thomas, Publisher, 1931, pp. 271 and 414; footnote 1*a*.

5. György, P.; Moro, E., and Witebsky, E.: Milchantikörper im Serum von Säuglingen, Klin. Wchnschr. **10**:821, 1931. Smyth, F. S., and Bain, K.: Enteral Absorption of the Antigen and the Apparent Failure of Antigen Secretion in Human Milk, J. Allergy **2**:282, 1931. Keller, W.: Ueber enterale Resorption, Klin. Wchnschr. **11**:855, 1932. Ratner, B., and Gruehl, H. L.: Passage of Native Proteins Through the Normal Gastro-Intestinal Wall, J. Clin. Investigation **13**: 517, 1934.

A CLINICAL COMPARISON OF THE ANTIRACHITIC VALUE OF IRRADIATED YEAST AND OF COD LIVER OIL

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This investigation was undertaken for the purpose of determining the amount of irradiated dry yeast necessary for the cure of rickets in children and of making a comparison of the antirachitic potency of such yeast with that of cod liver oil by means of clinical findings. Yeast, which is one of the richest known sources of ergosterol, is easily given antirachitic potency by means of exposure to ultraviolet rays. This study was carried out experimentally by Hess and his collaborators [1] in 1924, and although the products yielded encouraging results in the preliminary tests the therapeutic uses of irradiated yeast have not been clinically determined. Its advantages appear to be its relative cheapness and the ease with which it may be administered, on account of both its consistency and its flavor.

Few clinical tests of irradiated yeast have been made. Kon and Mayzner [2] in Warsaw, Poland, carried out a study in an institution on twelve rachitic children from 4 months to 2½ years old. Six of the subjects received daily doses of 0.75 Gm. of irradiated yeast (rat unit potency not stated), three received the same quantity of nonirradiated yeast and three continued on the usual institutional diet with no vitamin D supplement. From this study the investigators concluded that their preparation of irradiated yeast brought about a disappearance of symptoms in from six to eight weeks, as judged by chemical changes of the blood and roentgenograms.

The expense of the research was defrayed by a grant from The Quaker Oats Company, Chicago.

This project was carried out jointly in the laboratories of the Department of Surgery, Orthopedic Department, the University of Chicago Clinics, and of the Department of Home Economics and Household Administration, the University of Chicago.

1. Hess, A. F.: Ultra-Violet Irradiation, Irradiated Ergosterol, and Irradiated Food, Acta pædiat. **11**:1, 1930.

2. Kon, S. K., and Mayzner, M.: A Study of the Antirachitic Value of Irradiated Yeast, Lancet **1**:794, 1930.

As mentioned previously, however, the immediate interest in irradiated yeast had to do not only with its therapeutic uses but with its clinical efficacy directly compared with that of cod liver oil. Recent studies on animals in the laboratory and on patients in the clinic with regard to the numerous vitamin D preparations now available in this country have revealed that various products of equivalent antirachitic potency, as judged by the rat test, possess markedly different values for the treatment of other species—notably the chick and the human infant.

That viosterol and irradiated yeast are not so effective in the control of rickets in the chick as is cod liver oil when equivalent rat units of vitamin D are fed has been reported by Massengale and Nussmeier [3] and Bethke, Record and Kennard.[4] Further, Steenbock and his co-workers [5] reported that it required from 7.5 to 60 times as many rat units in irradiated yeast as in cod liver oil to produce the same degree of bone repair in chickens.

In emphasizing the differences in the effectiveness of the antirachitic factor in various species, Hess [1] made the following statement before the Second International Pediatric Congress in 1930:

> On the basis of equal weight, an infant requires about sixty times as much irradiated ergosterol as a rat and about twenty times as much cod liver oil. It will be noted that there is a ratio of 3 to 1 between the activity of cod liver oil and irradiated ergosterol. This same ratio has been found, in the course of clinical experience, to represent approximately the excess of irradiated ergosterol required to protect infants from rickets.

Some evidence from Hess' clinic indicates that irradiated milk is more efficient in the child than in the rat when cod liver oil is the basis of comparison. As stated in an editorial in *The Journal of the American Medical Association:*[6] "Such differences in effectiveness of the antirachitic factor in various species may be due to inherent difficulties in the biologic method of assay, to the widely differing types of food ingested by various species, to altered utilization of the vitamins because of possible variations . . . in the pathogenesis of rickets in different species." Still further it may be due to some such cause as that postulated by Wisconsin workers [5] that the vitamin D produced by ordinary

3. Massengale, O. N., and Nussmeier, M.: The Action of Activated Ergosterol in the Chicken: II. The Prevention of Leg Weakness, J. Biol. Chem. **87:** 423, 1930.

4. Bethke, R. M.; Record, P. R., and Kennard, D. C.: The Comparative Antirachitic Efficiency of Irradiated Ergosterol, Irradiated Yeast, and Cod Liver Oil for the Chicken, J. Nutrition **6:**413, 1933.

5. Steenbock, H.; Kletzien, S. W. F., and Halpin, J. G.: The Reaction of the Chicken to Irradiated Ergosterol and Irradiated Yeast as Contrasted with the Natural Vitamin D of Fish Liver Oils, J. Biol. Chem. **97:**249, 1932.

6. The Relative Efficiency of Vitamin D Preparations in Different Species, editorial, J. A. M. A. **99:**565 (Aug. 13) 1932.

irradiation of ergosterol with a quartz mercury vapor arc lamp may be a different substance from that found in cod liver oil.

METHODS

Regardless of the reasons underlying the differences in the efficacy of vitamin D from different sources for a given species, they can readily be compensated for by basing the doses of various preparations on experimental observations. It was planned in this study to determine values representing the degree of improvement brought about in the condition of rachitic children which would allow for a direct comparison of irradiated yeast with cod liver oil. In searching for subjects for our study, infants showing one or more clinical signs of rickets and subsisting on

TABLE 1.—*Analysis of the Physical Findings in Children with Rickets*

Subject	Age, Months	Sex	Race	Bosses		Beading of Ribs	Harrison's Groove	Flaring Ribs	Pot Belly	Widening			"Double Epiphysis"	Bowing of Legs	Enlarged Cervical Glands
				Frontal	Parietal					Wrists	Knees	Ankles			
1. J. A.	13	M	N	1*	1	3	2	2	2	2	2	0	0	1	2
2. L. R.	18	M	N	2	2	3	2	2	2	1	1	0	0	?	1
3. Ab. W.	18	M	N	2	1	3	1	1	2	1	1	0	0	1	1
4. M. M.	26	F	W	1	2	3	1	1	1	2	1	1	0	?	1
5. J. T.	17	F	N	0	1	3	0	?	2	3	1	0	L 1 R ?	0	0
6. C. L.	11½	M	N	0	1	2	3	3	2	1	0	0	0	?	1
7. J. R.	7	F	N	0	1	1	0	0	0	1	1	0	0	0	1
8. An. W.	26	M	N	0	1	2	0	0	0	0	0	0	0	0	0
9. J. P.	22	F	W	1	0	2	0	2	2	1	1	1	0	3	1
10. F. T.	10	M	N	0	0	2	0	0	1	2	0	0	0	?	R 3 L 1
11. J. H.	20	M	W	2	2	2	2	2	1	2	2	2	0	1	1
12. D. F.	26	M	N	1	3	2	3	3	2	1	2	1	0	3	2
13. Je. T.	17	F	N	1	2	2	0	1	2	1	1	0	0	1	0
14. F. Y.	13	M	W	0	0	1	0	0	0	0	0	0	0	?	1
15. J. B.	10	F	N	1	1	3	1	1	1	1	0	0	0	0	1
16. F. M.	19	M	N	1	1	1	0	0	1	1	1	0	0	?	?
17. R. M.	10	M	W	3	2	2	1	2	2	1	1	0	0	?	1
18. Y. W.	32	F	N	1	2	2	0	0	0	1	1	1	2	?	1
19. O. H.	11	F	N	0	2	1	1	2	3	1	1	0	0	?	1
20. V. W.	9	M	N	0	1	2	1	1	2	1	1	0	0	1	1
21. E. C.	12	F	W	2	3	1	2	2	2	1	1	1	0	1	1

* The key is as follows: ?, questionable; 0, absent; 1, mild or slight; 2, moderate, and 3, marked.

a diet deficient in the antirachitic vitamin were chosen. From a group of eighty-three infants referred to us by conference physicians in infant welfare stations in Chicago, twenty-one were selected for observation (table 1).

All but five of these children were colored; they ranged in age from 5 months to 2½ years and showed signs of rickets of different degrees of severity from doubtful to definitely active. They were housed from Jan. 1 to April 1, 1934, on the first floor of the Gertrude Dunn Hicks Memorial Hospital, which is part of the Orthopedic Department of the University of Chicago Clinics and is supported by the Home for Destitute Crippled Children.

None of the children received any direct sunlight or ultraviolet irradiation during the period of observation, and all were given the same care throughout the study. The rickets curve in the Great Lakes region ascends during January and reaches a peak about the first of March. These months were chosen for our study in order to rule out seasonal factors in the healing of rickets.

From conferences with the mothers of the subjects it was concluded that the children were, as a general rule, subsisting on a diet of milk supplemented with

carbohydrates, such as bread and cereals, and occasional vegetables and fruits. Accordingly, a basal diet was planned to approximate these findings as closely as possible. The food included whole cow's milk, cereal porridges, bread and potatoes, all of which could be taken ad libitum, 2 tablespoonfuls of puréed vegetable and 1 tablespoonful of fruit per day and 4 ounces (118.4 cc.) of orange juice per week. This diet was high in carbohydrates and rather low in vitamins; it was adapted in its character and manner of administration to the age of the subject.

After preliminary roentgenographic examination, chemical analysis of the blood and hospitalization for a period of not less than fifteen days the children were divided into five groups, an attempt being made to include in each group patients with each degree of rickets diagnosed and to distribute the ages as uniformly as possible through the groups. One group of four subjects was continued on the basal diet with no supplement; a second group of four was given three daily doses, totaling 10.5 Gm., of cod liver oil. This oil was composed of a mixture of equal portions of four well known brands, as purchased in the retail market. These constituted negative and positive control groups. The remaining three groups of four, four and five children, respectively, were given different quantities of irradiated powdered yeast. Preliminary estimations of the potencies of the two materials to be compared indicated that the cod liver oil probably contained about 108 and the irradiated yeast about 2,514 United States Pharmacopeia revised units per gram. Thus the expected potency ratio of the oil to the yeast was 1:23. On that premise the lowest level of yeast, 0.417 Gm. per day, was established to equal the estimated rat unitage of 10.5 Gm. of cod liver oil. The other amounts (1.251 and 2.502 Gm. per day) were arbitrary threefold and sixfold multiples of the minimum quantity. Bio-assays on rats conducted by Dr. W. C. Russell of Rutgers University and terminated after the clinical test indicated potencies of 192 U. S. P. units for the cod liver oil and 5,400 U. S. P. units per gram for the irradiated yeast. The ratio of the measured potencies was 1:28. According to the bio-assays, the 10.5 Gm. of cod liver oil administered daily contained 2,016 units and the quantities of irradiated yeast 2,252, 6,755 and 13,511 U. S. P. units, respectively. The yeast was given to the children in some article of diet, such as puréed vegetable, fruit or cereal.

The criteria used in judging the condition of the children were as follows: (1) maintenance of, or gain over, the body weight at the beginning of treatment, as determined by weekly measurement of weight taken by a standard procedure; (2) changes in the level of serum calcium and phosphorus, from samples of the blood taken at intervals of not less than fourteen days, and (3) changes in the calcification of the bones of the wrists and forearms as shown in roentgenograms recorded at regular intervals. The serum calcium was determined by the Clark-Collip modification of the Kramer-Tisdall method [8] and the phosphorus by the Fiske and Subbarow colorimetric procedure.[9] The figures presented are the average of at least duplicate analyses agreeing within 3 per cent.

In addition to this program, the retention of calcium and phosphorus was determined for simultaneous periods of twenty days on three of the subjects. The three children selected were subject 1, a child receiving the basal diet with no vitamin D supplement, subject 6, who was in the group receiving cod liver oil, and subject 17, who received the maximum quantity of irradiated yeast.

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7. This footnote was deleted by the author.

8. Clark, E. P., and Collip, J. B.: A Study of the Tisdall Method for the Determination of Blood Serum Calcium with a Suggested Modification, J. Biol. Chem. **63**:461, 1925.

9. Fiske, C. H., and Subbarow, Y.: The Colorimetric Determination of Phosphorus, J. Biol. Chem. **66**:375, 1925.

The treatment during the time that the children were on the metabolism beds was exactly the same in each case as it was throughout other periods in the study except that the intake of food was weighed, with an aliquot portion representing one fifth of the total consumption being dried and ground for analysis (fig. 12). These samples of food as well as urine and feces collected for corresponding periods were treated and analyzed for calcium and phosphorus according to a manner described elsewhere.[10]

OBSERVATIONS

There was no serious illness in the entire group during the period of observation, although an occasional mild infection of the upper respiratory tract accompanied by fever and loss of appetite was recorded. All the children showed some gain in weight, the increase ranging from

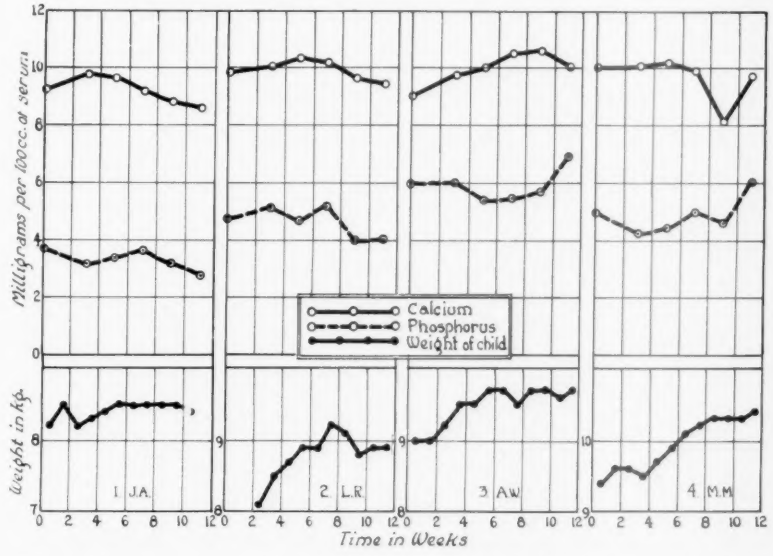

Fig. 1 (group I).—Record of weight and serum calcium and phosphorus content for the group receiving the basal diet and no vitamin D supplement. In this negative control group only one of the patients (subject 3) showed any improvement from the standpoint of calcium and phosphorus content. Each of the patients showed a satisfactory gain over the initial weight. Subject 1, in whom the rickets was more severe, showed a definite decrease in both the calcium and the phosphorus content, and the weight gained was less than in the others.

0.1 to 1.2 Kg., with an average increment of 0.8 Kg. The weight curves (figs. 1 to 5) indicate that the caloric intake of the subjects was reasonably adequate. The yeast was easily given and very well tolerated, no gastro-intestinal disturbances occurring even in the group receiving the maximum amount.

10. Porter-Levin, T.: Calcium and Phosphorus Metabolism of Normal Pre-School Children: II. Successive Balance Studies, J. Am. Dietet. A. **9**:22, 1933.

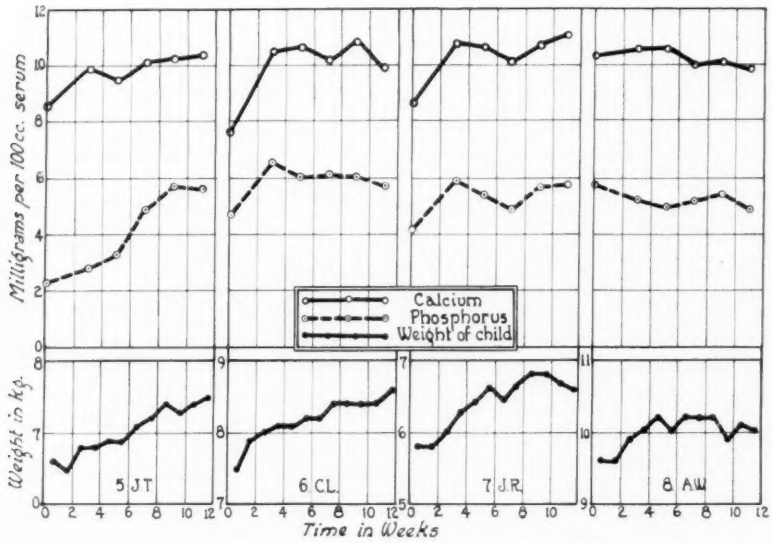

Fig. 2 (group II).—Record of weight and serum calcium and phosphorus content for the group receiving the basal diet and 10.5 Gm. of cod liver oil daily. All the patients except subject 8 showed a rise in both the calcium and the phosphorus content, and all showed a satisfactory gain in weight.

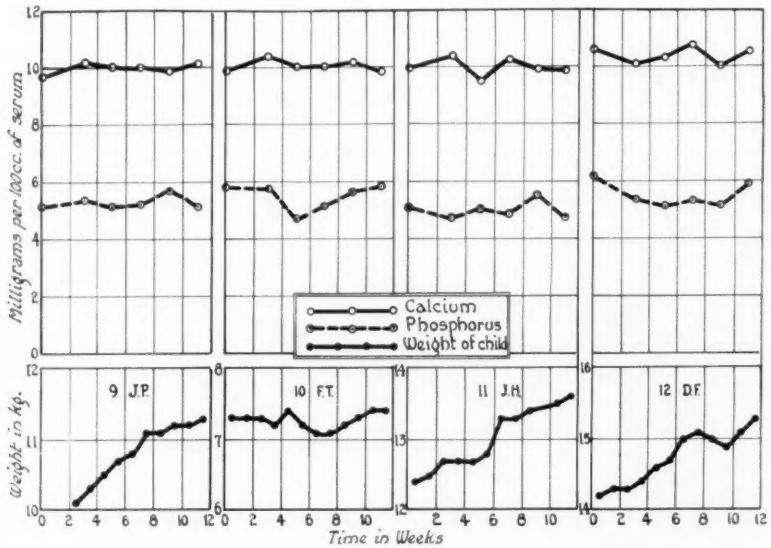

Fig. 3 (group III).—Record of weight and serum calcium and phosphorus content for the group receiving the basal diet and 0.417 Gm. of irradiated yeast daily. There was no consistent change in either the calcium or the phosphorus content in any patient in this group in which the minimal amount of irradiated yeast was given. Each patient, however, with the exception of subject 10, in whom the gain in weight was insignificant, showed an increase in body weight during the course of the experiment.

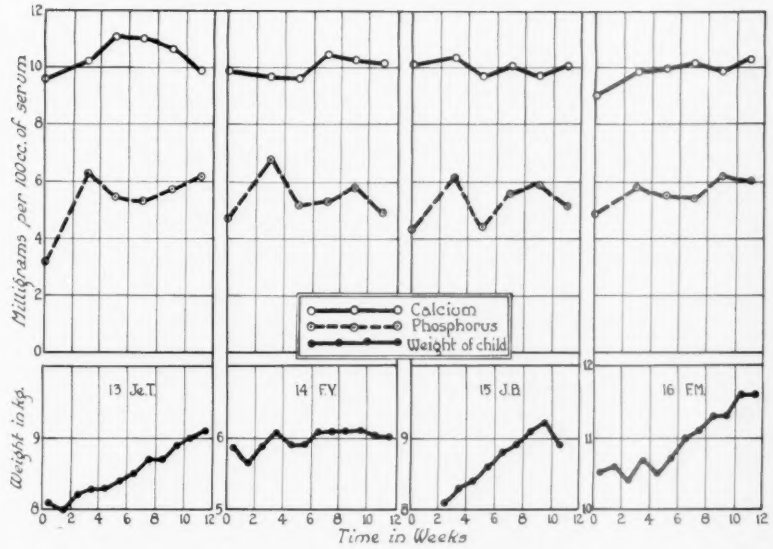

Fig. 4 (group IV).—Record of weight and serum calcium and phosphorus content of the group receiving the basal diet and 1.251 Gm. of irradiated yeast daily. The patients in this group, receiving the intermediate amount of irradiated yeast, all gained weight. There was no consistent change in the calcium content, but each patient showed an increase in the content of phosphorus. This was most marked in subject 13, who had very active rickets at the beginning of the experiment.

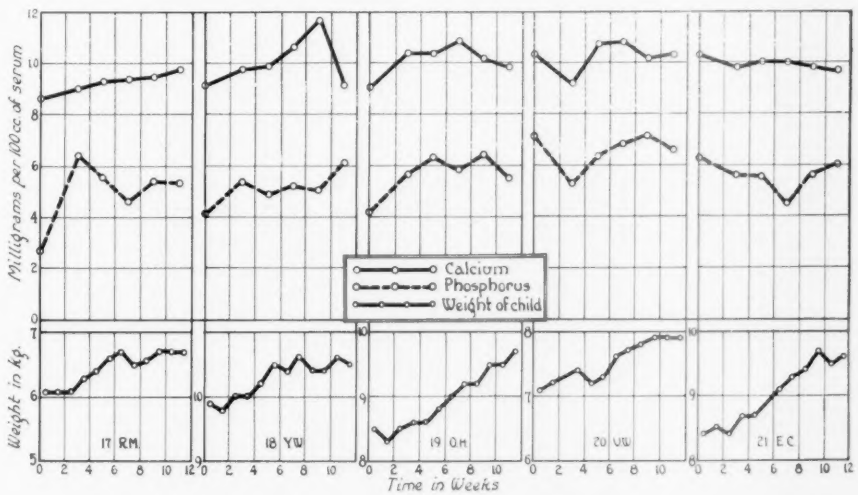

Fig. 5 (group V).—Record of weight and serum calcium and phosphorus content for the group receiving the basal diet and 2.502 Gm. of irradiated yeast daily. The five patients in this group received the maximum amount of irradiated yeast. Each patient made a consistent and satisfactory gain in weight. There was a definite increase in the content of phosphorus and, with the exception of subject 21, of the calcium content as well. From the standpoint of the blood chemistry and of the weight curve the patients in this group showed the most satisfactory improvement.

Chemical Analysis of the Blood.—In general, it may be said that the levels of calcium and phosphorus tended toward low or low normal values at the time our observations were begun. The calcium-phosphorus products accordingly fell below 60; the subjects with the most marked rickets in each group showed the lowest values, 30 or below. There were, however, patients with clinical and roentgen evidence of active or unhealed rickets who had a calcium-phosphorus product between 50 and 60. An examination of all the values for blood serum in table 2 and figures 1 to 5 reveals that within each group the children with the more severe rickets responded best. For example, subject 1, the negative control in group I, showed a consistent decrease in serum calcium and phosphorus with a fall in the calcium-phosphorus product from 35 to 24. In the opposite manner, subjects 5, 13 and 17, children with marked rickets receiving some form of vitamin D, each showed the greatest increase in the calcium-phosphorus product of any of the other subjects in their respective groups.

In order to arrive at some basis for evaluating the change which occurred in each subject and in each group as a whole during the experiment the percentage of change (±) in the values for calcium and phosphorus and the calcium-phosphorus product were calculated, two values being used, the one determined at the beginning and the one determined at the end of the period of observation. These changes are graphically represented in figure 6. The following results were obtained in the individual groups.

Group I (No Vitamin D): In three subjects the calcium values and in two the phosphorus values were decreased while in the remaining subjects in the group the values were slightly increased (fig. 6 *A* and *B*). The group as a whole showed a slight retrogression, as judged by an average decrease of 1 per cent in the calcium-phosphorus product. This leads to the conclusion that our methods of handling the subjects did not induce any significant change in their rachitic condition by initiating spontaneous healing.

Group II (Cod Liver Oil): This group included three children whose serum mineral values were significantly increased and a fourth whose mineral values were decreased. The fourth subject, in whom there was a decrease in the calcium-phosphorus product (fig. 6 *C*), had the mildest rickets in the group. As a whole, however, this group showed significant improvement in the levels of both calcium (19 per cent) and phosphorus (46 per cent).

Group III (0.417 Gm. Irradiated Yeast): The subjects in this group showed considerable variation in response to the treatment. As a whole the calcium values for the group showed no significant change (+1 per cent); the phosphorus values likewise remained about the same

(— 3 per cent), with a consequent calcium-phosphorus product of unchanged value (fig. 6). Although there was no marked evidence of improvement in the blood chemistry the roentgenograms of the patient with definitely active rickets (subject 9) showed a response.

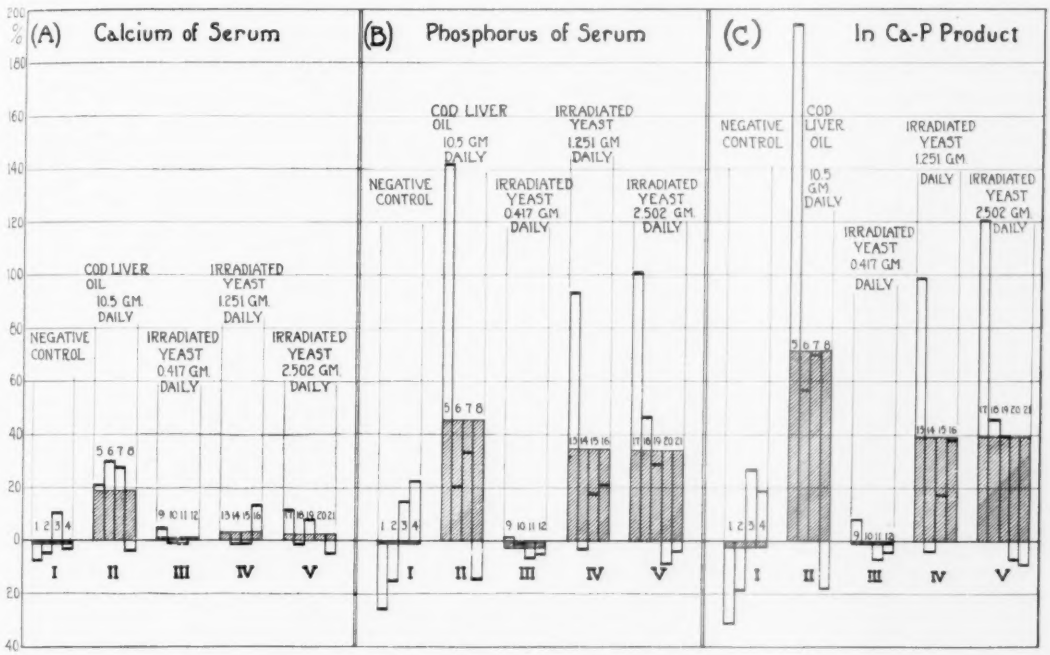

Fig. 6.—Record of the percentage of change in the calcium and inorganic phosphate content of the serum and in the calcium-phosphorus product for each patient. The columns of diagonal lines indicate the average change for each group, and the open columns, the change for each subject. As will be noted in *A*, only in group II was there a significant increase in the calcium content. This occurred in three of the subjects, while subject 8 showed a decrease in the calcium content. The average for the group, however, was about a 19 per cent increase. In group I there was an average decrease in calcium content and an insignificant increase in each of the groups receiving irradiated yeast. In *B* it will be seen that there was a decrease in the inorganic phosphate content in subjects 1 and 2 of group I and an increase in subjects 3 and 4, but an average decrease for the group. Three of the patients in group II showed a satisfactory increase in inorganic phosphate content. The increase in subject 5, who had the most active rickets, was more than 135 per cent, while the average increase for the group was 45 per cent. There was no increase in the inorganic phosphate content in any of the subjects in group III; there was an average decrease of about 3 per cent. All the subjects in group IV showed some rise in the inorganic phosphate content but, as was true in groups II and V, a marked rise was noted only in the subjects with very active rickets. The average increase for both group IV and group V was satisfactory, however. Although we do not feel that the calcium-phosphorus product (*C*) is as important as it was formerly thought to be, it is interesting to note that it was markedly increased in group II and satisfactorily increased in groups IV and V, while there was an average decrease in the product in groups I and III.

TABLE 2.—*Serum Calcium and Phosphorus Values and Roentgen Observations on the Wrists of Twenty-One Rachitic Children Studied for a Period of Ten Weeks*

Name	Age, Months	Race	Clinical Evidence of Severity of Rickets	Weight, Kg.	Date	Calcium, Mg. per 100 Cc.	Phosphorus, Mg. per 100 Cc.	Calcium-Phosphorus Product	Roentgen Observations on Bones of Wrist	
									Before Beginning Treatment	End of Treatment
Group I: no supplement										
1. J. A.	11	N	Marked	8.2 to 8.4	1/15	9.32	3.72	34.68	1/5: cupping, widening and some absorption in distal end of radius and ulna; shaft rarefied	3/30: bones still osteoporotic; more absorption in juxta-epiphyseal region
					2/ 5	9.83	3.16	31.06		
					2/19	9.59	3.43	32.89		
					3/ 5	9.24	3.68	34.00		
					3/18	8.76	3.20	28.03		
					4/ 1	8.57	2.77	23.74		
2. L. R.	16	N	Moderate	8.0 to 8.9	1/15	9.92	4.74	47.02	1/3: cupping, flaring, thinning of distal end of radius and ulna; thin cortex	3/30: same condition as on 1/3; possibly less ossification
					2/ 5	10.05	5.14	51.66		
					2/19	10.30	4.68	48.20		
					3/ 5	10.19	5.18	52.78		
					3/18	9.64	4.00	38.56		
					4/ 1	9.46	4.02	38.03		
3. Ab. W.	16	N	Mild	9.0 to 9.7	1/15	9.08	6.04	54.84	1/3: doubtful flaring of distal end of radius and ulna; rarefaction of juxta-epiphyseal portion and shaft	3/30: same degree of density of shafts; more cupping and absorption at distal end of ulna
					2/ 5	9.75	6.04	58.90		
					2/19	10.02	5.43	54.41		
					3/ 5	10.52	5.48	57.65		
					3/18	10.61	5.66	60.05		
					4/ 1	10.09	6.95	70.13		
4. M. M.	24	W	Mild	9.4 to 10.4	1/15	10.00	4.96	49.60	1/10: doubtful flaring and irregular absorption in distal end of ulna; no rarefaction of shafts	3/30: slightly more evidence of absorption, but no definite rickets
					2/ 5	10.05	4.28	43.01		
					2/19	10.18	4.37	44.49		
					3/ 5	9.96	4.98	49.60		
					3/18	8.11	4.55	36.90		
					4/ 1	9.66	6.10	58.93		
Group II: cod liver oil (10.5 Gm. per day)										
5. J. T.	15	N	Marked	6.6 to 7.5	1/15	8.52	2.30	19.60	1/6: marked osteoporosis of radius, ulna and bones of hands; cortex indistinct; cupping, fraying, flaring of distal end of shaft	3/30: cupping of ulna marked; increased density in shaft; slight rounding off of distal end of left radius; more normal bone structure in juxta-epiphyseal portion
					2/ 5	9.92	2.96	29.36		
					2/19	9.50	3.26	30.97		
					3/ 5	10.15	4.94	50.14		
					3/18	10.28	5.62	57.77		
					4/ 1	10.33	5.59	57.74		
6. C. L.	10	N	Mild	7.5 to 8.6	1/15	7.31	4.74	34.64	12/19: marked widening of distal end of radius and ulna; cupping and irregular rarefaction of ulna; increased density in juxta-epiphyseal portion; osteoporotic shaft; thin cortex	3/30: marked density of radius; some absorptive changes in distal end of ulna
					2/ 5	10.00	6.56	65.60		
					2/19	10.18	6.03	61.39		
					3/ 5	9.67	6.16	59.57		
					3/18	10.38	6.13	63.63		
					4/ 1	9.53	5.71	54.42		
7. J. R.	5	N	Moderate	5.8 to 6.6	1/15	8.65	4.24	36.68	1/9: doubtful flaring, cupping of distal end of radius and ulna; possible absorption in distal end of ulna; some osteoporosis	3/30: normal density in shafts of radius and ulna
					2/ 5	10.80	5.86	63.29		
					2/19	10.61	5.44	57.72		
					3/ 5	10/15	4.83	49.02		
					3/18	10.66	5.62	59.91		
					4/ 1	11.10	5.68	63.05		

8. An. W.	24	N	Very mild	9.6 to 10.0	1/15	10.30	5.74	59.12	1/5: slight absorption in juxta-epiphyseal portion of radius and ulna; moderate flare of distal end; shaft fairly normal	3/30: no definite changes
					2/ 5	10.52	5.24	55.12		
					2/19	10.52	4.98	52.39		
					3/ 5	10.00	5.17	51.70		
					3/18	10.14	5.41	54.86		
					4/ 1	9.89	4.90	48.46		
Group III: irradiated yeast (0.417 Gm. per day)										
9. J. P.	30	W	Marked	10.1 to 11.3	1/15	9.68	5.16	49.95	1/3: slight widening at distal end of radius and ulna; slight absorption in juxta-epiphyseal portion; metaphysis of radius approximately twice as wide as diameter of shaft	3/30: radius normal; still slight flaring of juxta-epiphyseal portion; distal end of ulna less dense than normal
					2/ 5	10.23	5.38	55.04		
					2/19	10.08	5.18	52.21		
					3/ 5	10.05	5.23	52.56		
					3/18	9.90	5.72	56.63		
					4/ 1	10.21	5.26	53.70		
10. F. T.	8	N	Moderate	7.3 to 7.4	1/15	9.92	5.86	58.12	1/3: marked flaring and irregularity of juxta-epiphyseal portion; epiphysis of radius and ulna have not appeared; osteoporosis; cortex indistinct	3/30: juxta-epiphyseal portion sharp and distinct; no cupping; persisting flaring
					2/ 5	10.42	5.90	61.48		
					2/19	10.02	4.65	46.59		
					3/ 5	10.01	5.23	52.35		
					3/18	10.19	5.62	57.27		
					4/ 1	9.87	5.83	57.54		
11. J. H.	18	W	Mild	12.4 to 13.6	1/15	10.00	5.10	51.00	1/3: questionable zone of rarefaction at distal end of right radius; shaft rather well ossified; doubtful evidence of rickets	3/30: zone of increased density of the end shaft of radius
					2/ 5	10.44	4.72	49.28		
					2/19	9.50	5.08	48.26		
					3/ 5	10.33	4.94	51.03		
					3/18	9.95	5.64	56.12		
					4/ 1	9.89	4.76	47.08		
12. D. F.	24	N	Very mild	14.2 to 15.3	1/15	10.53	6.22	65.50	1/5: slight flaring and slight absorption in distal end of radius and ulna; cortex thin; doubtful evidence of rickets	3/30: slight decrease in density; slight cupping of distal end of ulna; radius normal
					2/ 5	10.13	5.40	54.70		
					2/19	10.35	5.16	53.41		
					3/ 5	10.77	5.34	57.51		
					3/18	10.05	5.20	52.26		
					4/ 1	10.54	5.92	62.40		
Group IV: irradiated yeast (1.251 Gm. per day)										
13. Je. T.	15	N	Marked	8.1 to 9.1	1/15	9.61	3.20	30.76	1/10: marked flaring and cupping of distal end of radius and ulna; irregular ossification in metaphysis; osteoporosis in shaft	3/30: marked healing and almost normal appearance in juxta-epiphyseal portion of radius and ulna; radius sharply defined at distal end; slight absorption in ulna
					2/ 5	10.20	6.34	64.66		
					2/19	11.09	5.48	60.77		
					3/ 5	11.00	5.31	58.41		
					3/18	10.60	5.68	60.21		
					4/ 1	9.89	6.20	61.32		
14. F. Y.	11	W	Moderate	5.9 to 6.0	1/15	9.67	5.12	49.51	12/26: moderate flaring of metaphysis of radius and ulna; absorption in juxta-epiphyseal portion of ulna; mild cupping; questionable osteoporosis in shaft	3/30: increased density in juxta-epiphyseal portion of ulna; juxta-epiphyseal portion of radius normal; left wrist normal; mild absorption in distal end of right ulna
					2/ 5	9.72	6.74	65.52		
					2/19	9.56	5.20	49.71		
					3/ 5	9.95	5.31	52.83		
					3/18	9.71	5.80	56.32		
					4/ 1	9.61	4.93	47.38		
15. J. B.	8	N	Mild	8.0 to 8.9	1/15	10.10	4.38	44.24	12/19: slight flaring of distal end of radius and ulna; absorption in juxta-epiphyseal portion of ulna; slight osteoporosis in shaft; cortex thin	3/30: persisting flaring of distal end of radius and ulna; left wrist normal; mild cupping, absorption in right ulna
					2/ 5	10.32	6.18	63.78		
					2/19	9.72	4.43	43.06		
					3/ 5	10.05	5.55	55.78		
					3/18	9.71	5.85	56.80		
					4/ 1	10.02	5.19	52.00		

Group IV (1.251 Gm. Irradiated Yeast): The group as a whole showed no significant change in the values for calcium (+ 4 per cent), but the values for phosphorus increased markedly in every subject (+ 33 per cent). The calcium-phosphorus product was improved by 39 per cent (fig. 6). Irradiated yeast in adequate amounts has been shown previously [2] to have a noticeable effect on the phosphorus level in rachitic patients.

Group V (2.502 Gm. Irradiated Yeast): The subjects showed greater individual fluctuation in values than those in group IV, but as a whole the response was the same, with the calcium content increased by 3 per cent and the phosphorus content by 33 per cent. The calcium-phosphorus product was improved by 39 per cent (fig. 6).

Roentgen Studies.—Roentgenograms of the wrists of each patient were made before admission to the hospital, at the time of beginning the experimental study and at intervals of from two to three weeks throughout the period of observation. The grouping of the patients was based more on the interpretations of the roentgenograms than on the chemical values of the blood. The degree of rickets varied from mild or doubtful activity with poor ossification of the shafts of the bones and indefinite lines of bone formation in the juxta-epiphyseal region to marked osteoporosis of the shafts and cupping and fraying of the metaphyseal portions of the bones in the most active cases.

Table 2 contains a brief analysis of the significant changes noted in the series of roentgenograms for each child during the course of the study.[11]

Roentgenograms of each of the subjects in the negative control group (group I) showed slightly more osteoporosis and fraying in the juxta-epiphyseal regions of the bones of the forearm at the end of the period of observation than they did at the beginning of the experiment (fig. 7).

Improvement was noted in the roentgenograms of these patients in group II after three months' treatment with 10.5 Gm. of cod liver oil daily. The child with the most marked rickets in the group (subject 5) still showed cupping of the distal end of the ulna and radius and fraying in the juxta-epiphyseal region, which was evidence of incomplete healing of the rickets (fig. 8).

The roentgenograms of three of the patients receiving the minimal supplement of irradiated yeast (group III) showed no definite changes during the period of observation. The roentgenograms of the wrists of the subjects in this group with the most active rickets (subject 9) showed progressive improvement, and after three months' treatment

11. These roentgenograms were studied in consultation with Dr. Martha Eliot, Assistant Chief of the Children's Bureau of the United States Department of Labor, and Dr. Grover Powers, Professor and Chairman of the Department of Pediatrics, of Yale Medical School.

TABLE 2.—*Serum Calcium and Phosphorus Values and Roentgen Observations on the Wrists of Twenty-One Rachitic Children Studied for a Period of Ten Weeks—Continued*

Name	Age, Months	Race	Clinical Evidence of Severity of Rickets	Weight, Kg.	Date	Calcium, Mg. per 100 Cc.	Phosphorus, Mg. per 100 Cc.	Calcium-Phosphorus Product	Roentgen Observations on Bones of Wrists	
									Before Beginning Treatment	End of Treatment
16. F. M.	18	N	Very mild	10.5 to 11.6	1/15	9.05	4.94	44.70	1/11: slight flaring of distal end of left ulna; slight absorption in juxta-epiphyseal portion of ulna; fair ossification in shaft	3/30: radius same; little more absorption in shaft of ulna
					2/ 5	9.86	5.84	57.58		
					2/19	9.99	5.54	55.34		
					3/ 5	10.22	5.46	55.80		
					3/18	9.90	6.20	61.38		
					4/ 1	10.32	6.01	62.02		
Group V: irradiated yeast (2.502 Gm. per day)										
17. R. M.	8	N	Marked	6.1 to 6.7	1/15	8.65	2.68	23.18	1/3: marked flaring, cupping, irregular ossification and absorption in distal end of radius and ulna; rarefaction in shaft; cortex very thin; no ossification centers for radius or carpal bones	3/30: marked improvement, with approximately normal ossification in radius and shaft of ulna; persisting widening of juxta-epiphyseal portion
					2/ 5	9.00	6.44	57.96		
					2/19	9.26	5.53	51.21		
					3/ 5	9.29	4.58	42.55		
					3/18	9.47	5.46	51.71		
					4/ 1	9.68	5.40	52.27		
18. Y. W.	30	N	Moderate	9.9 to 10.5	1/15	9.24	4.14	38.26	1/3: marked flaring and slight absorption in radius; slight cupping of ulna; zone of increased density in juxta-epiphyseal portion of radius; cortex thin	3/30: more normal ossification in distal end of radius and ulna; less sharply increased zones of density; cortex thin
					2/ 5	9.75	5.42	52.84		
					2/19	9.94	4.96	49.30		
					3/ 5	10.62	5.17	54.91		
					3/18	11.71	5.06	59.25		
					4/ 1	9.15	6.10	55.82		
19. O. H.	11	N	Moderate	8.5 to 9.7	1/15	9.08	4.26	38.68	1/3: widening of distal end of radius and ulna; irregular ossification in juxta-epiphyseal portion; slight cupping of ulna; rarefaction in shaft	3/30: same as earlier findings
					2/ 5	10.48	5.70	59.74		
					2/19	10.45	6.42	67.09		
					3/ 5	10.86	5.77	62.66		
					3/18	10.23	6.49	66.39		
					4/1	9.82	5.51	54.11		
20. V. W.	7	N	Very mild	7.1 to 7.9	1/15	10.30	7.20	74.16	1/5: slight flaring of distal end of radius and ulna with moderate absorption; metaphysis fairly well ossified; moderate osteoporosis of shaft; cortex thin; doubtful evidence of rickets	3/30: essentially normal
					2/ 5	9.29	5.38	49.98		
					2/19	10.70	6.44	68.91		
					3/ 5	10.77	6.85	73.77		
					3/18	10.28	7.23	74.32		
					4/1	10.42	6.55	68.25		
21. E. C.	10	W	Mild	8.4 to 9.6	1/15	10.34	6.32	65.34	1/11: moderate flaring of distal end of radius and ulna; absorption in juxta-epiphyseal portion; no cupping; little evidence of rickets	3/30: increased density in juxta-epiphyseal portion of radius
					2/ 5	9.83	5.62	55.24		
					2/19	10.08	5.55	55.94		
					3/ 5	10.06	4.53	45.57		
					3/18	9.85	5.70	56.14		
					4/ 1	9.77	6.06	59.21		

Fig. 7 (subject J. A., 11 months, group I, negative control).—The baby was breast fed and had never received any cod liver oil. *A*, made on admission, shows moderately active rickets, with cupping of the ulna and absorptive changes in the distal end of the radius. A zone of irregularly increased density in the juxta-epiphyseal portion suggests a minimal tendency toward healing. *B*, made one month later, shows changes almost identical with those previously described. *C*, taken four months from the time of the first observation, shows cupping and fraying of the distal end of the ulna as in the previous roentgenograms. There is no definite change in the radius. The shafts of the bones are still atrophic. The center of ossification of the radial epiphysis is not apparent, although the patient was 14 months of age. There was a slight difference in the roentgenographic technic in the last film, but no evidence of improvement can be seen. In this and figures 8, 9, 10 and 11 the roentgenograms to the left are of the left hand and those to the right are of the right hand.

Fig. 8 (subject 5, J. T., 15 months, group II, cod liver oil, 10.5 Gm. daily).—This child had markedly active rickets. *A* shows a marked degree of cupping of the distal ends of the radius and ulna, with fraying and poor ossification of the shafts of both bones. The cortex of the bone is thin and the medullary portion is proportionately widened. The center of ossification for the distal end of the radius has not appeared. *B*, made one month after the cod liver oil supplement was begun, shows less fraying, less cupping and better ossification of the shafts of the bones. *C*, made four months after treatment was begun, shows that cupping is still present but is much less than in the previous roentgenograms. The center of ossification of the radial epiphysis is well developed. There is some fraying at the distal ends of the bones, and a zone of irregular and dense calcification is seen in the juxta-epiphyseal region. The shafts of the bones are better ossified, and periosteal new bone has formed which increases the width of the shaft from 30 to 50 per cent. This roentgenogram shows definite but incomplete healing.

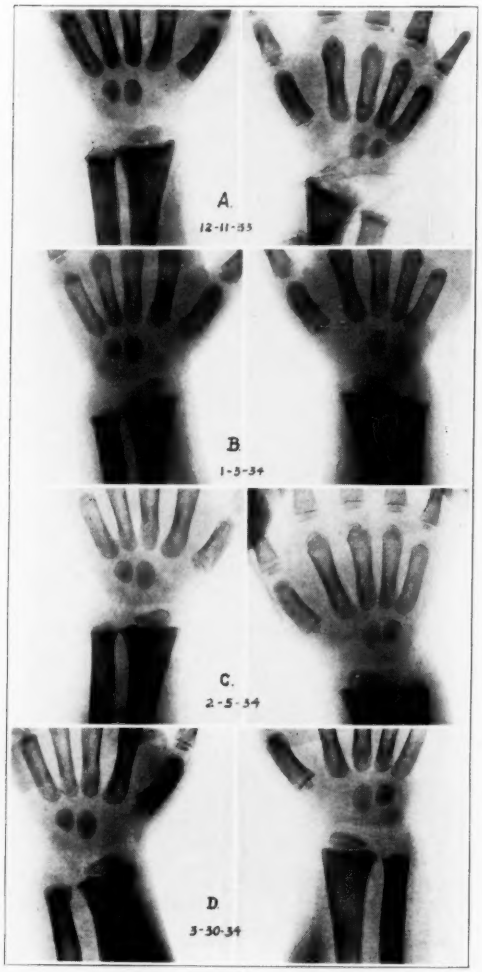

Fig. 9 (subject 9, J. T., 30 months, group III, irradiated yeast, 0.417 Gm. daily).—*A* is a roentgenogram taken on admission three weeks before the vitamin D supplement was begun. The metaphyses of the bones are widened and there is cupping of both the radius and the ulna with some fraying. There is, however, a definite zone of increased calcification in the juxta-epiphyseal region denoting that a healing process is present. This may be explained by the fact that until a month before this child was seen cod liver oil had been irregularly administered. A different roentgenographic technic was used in *B*, but further evidence of healing is noted. The supplement of irradiated yeast was begun at this time. *C* and *D* are roentgenograms taken one month and four months, respectively, after the supplement was begun. The radius appears to be normal, but there is less than normal ossification in the juxta-epiphyseal portion of the ulna.

there was roentgenographic evidence of healed rickets (fig. 9). This patient had received cod liver oil until two months before admission, which may explain the healing noted between Dec. 11, 1933, and Jan. 3, 1934, before the supplement was added.

Complete healing with restoration of the normal roentgenographic appearance of the bones was observed in each patient given the intermediate amount of irradiated yeast supplement (group IV). The improvement in the ossification of the shaft of the bones is well illustrated and the metaphyseal ends are sharply defined in figure 10.

The effectiveness of irradiated yeast in bringing about roentgenographic evidence of healing of rickets was well demonstrated in the subjects in group V (fig. 11), receiving 2.5 Gm. of the supplement daily, but the healing was no more rapid than when 1.25 Gm. was administered, as in group IV. This suggests that the optimum dosage of the product used in this experiment for the cure of rickets is not more than 1.25 Gm. daily and probably lies between that figure and the minimal amount used in group III (0.417 Gm.).

Marked roentgenographic changes were noted only in the cases of severe rickets. The number of children with active rickets was too small to draw definite conclusions, but in this series the roentgenograms of the wrists of the subjects with the more active rickets showed a quicker healing response to the feeding of irradiated yeast in any of the three dosages used and a more normal appearance of the bones after three months of treatment than did the subject with severe rickets (subject 5), who was treated with cod liver oil.[12]

Calcium and Phosphorus Balances.—The results of the determinations of balance showed that the child receiving no vitamin D supplement was storing a minimum amount of both calcium and phosphorus. The retention of phosphorus in this patient amounted to 9 per cent, and the retention of calcium to only 3 per cent, of the quantity ingested. The columns in figure 12 show the great quantities of calcium in the feces and the minute quantities in the urine of this rachitic subject. On the contrary, the two subjects receiving vitamin D, either as cod liver oil or as the maximum quantity of yeast, stored a significant amount of both calcium and phosphorus. The phosphorus retained represented 37 per cent of the intake in the subject receiving cod liver oil, and the calcium retained, 55 per cent of the intake. Results of the same order of magnitude were found in the patient receiving the maximum level of yeast, in whom 39 per cent of the phosphorus intake and 58 per cent of the calcium intake were retained. For these two last-mentioned patients receiving vitamin D and showing high retention of mineral, the excre-

12. We agree with Dr. Eliot, Dr. Powers and Dr. Frederick Tisdall, of the University of Toronto, who have expressed to us their belief that roentgenograms are the best means of studying the healing of rickets.

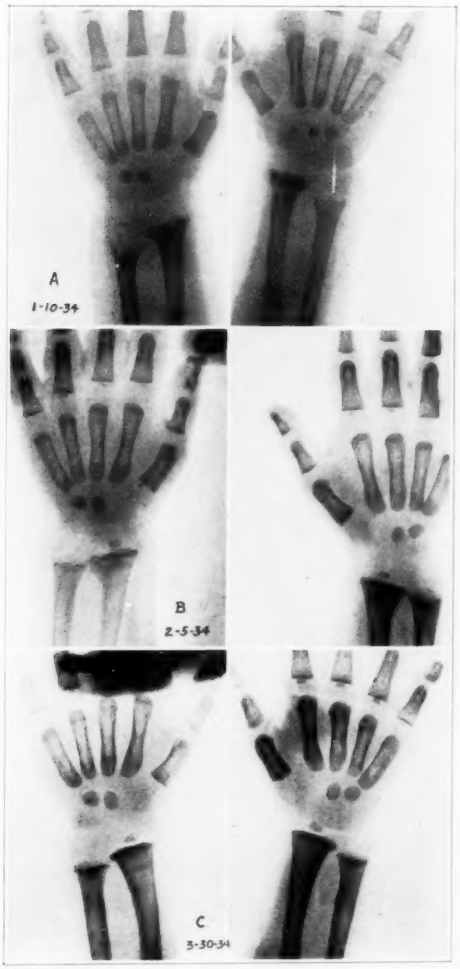

Fig. 10 (subject 13, Je. T., 15 months, group IV, irradiated yeast, 1.251 Gm. daily).—This patient was the twin sister of subject 5, who was treated with cod liver oil; the degree of rickets was similar. *A* shows markedly active rickets, with cupping of both the radius and the ulna and fraying in the juxta-epiphyseal portions. The center of ossification of the radial epiphysis has not appeared. The shafts of the bones are rarefied. *B*, taken one month after the supplement was begun, shows definite evidence of healing. There is less cupping, less fraying and some irregular calcification in the juxta-epiphyseal portions. The shafts of both bones are slightly wider than at the time of beginning the study. *C*, taken four months after the irradiated yeast was begun, shows complete healing of the rickets. There is a distinct, well ossified zone at the end of the shaft of both bones. The center of ossification of the radial epiphysis which appeared one month after beginning the supplement is now well developed. The cortex of the shaft of each bone of the forearm is of approximately normal thickness.

Fig. 11 (subject 17, R. M., 8 months, group V, irradiated yeast, 2.502 Gm. daily).—*A*, taken when the supplement was begun, shows marked flaring of the metaphysis of both bones of the forearms, cupping and fraying and incomplete ossification of the shafts of the bones. *B*, taken one month after the supplement was begun, shows definite evidence of healing. There is less cupping and fraying and a zone of increased density is apparent in the juxta-epiphyseal region. *C*, taken four months after the supplement was begun, shows the shafts of the bones at the wrist with normal density. There is a sharply defined line of ossification in the juxta-epiphyseal region and no cupping or flaring of the radius. A suggestion of cupping is still present in the distal end of the ulna. A series of six roentgenograms taken at intervals of from two to three weeks showed the healing of the rickets through normal ossification, and there was less irregular calcification in the juxta-epiphyseal portion at any time than was noted in subject 5, who was treated with cod liver oil.

tion of mineral through the feces was greatly reduced and that through the urine was somewhat increased when compared with the excretions of the subject used as a negative control. These results completely support the roentgen and blood chemistry observations in each of these cases (compare the data in figure 12 with the evidence for the same subjects in the roentgenograms and in figure 6).

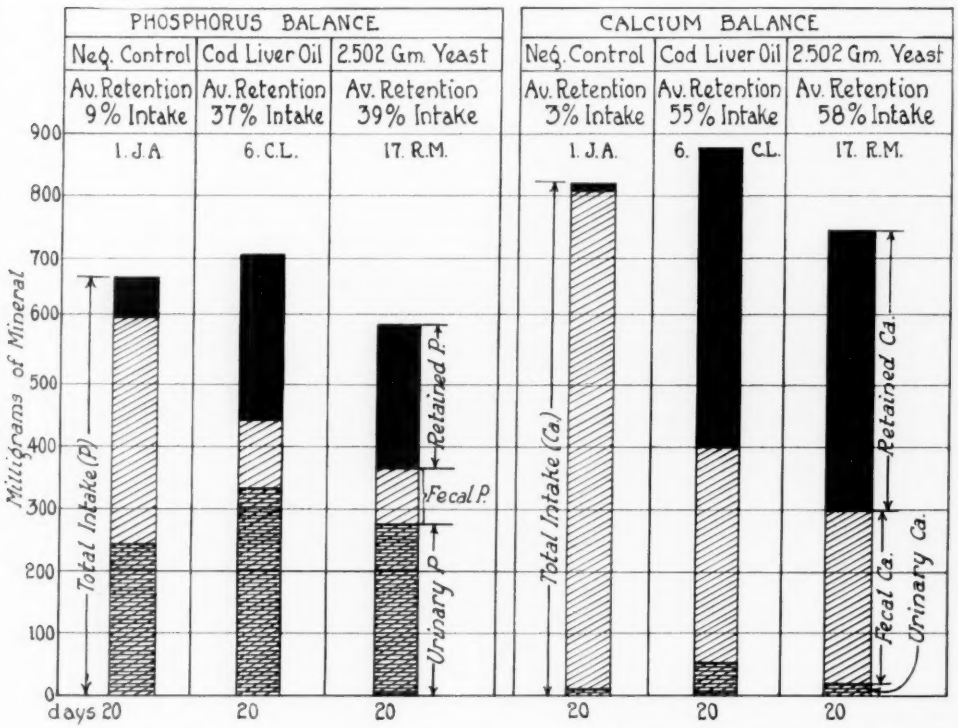

Fig. 12.—Record of the calcium and phosphorus balance over a period of twenty days with determinations made at five day intervals on three of the subjects with active rickets—one taken from the negative control group (subject 1), one from the group receiving cod liver oil (subject 6) and one from the group receiving the maximal amount of irradiated yeast (subject 17). The average retention of inorganic phosphates in the negative control patient was only 9 per cent while that in the patient receiving cod liver oil was 37 per cent of the intake and that in the patient receiving irradiated yeast, 39 per cent. It is interesting to note that the urinary calcium in these three patients did not vary greatly. The principal difference between the two groups lay in the fecal excretion of phosphorus and calcium. This suggests, although it does not prove, that the patient not receiving the vitamin D supplement was not absorbing from the gastro-intestinal tract a normal amount of calcium and phosphorus. An even more striking difference was noted with regard to the calcium retention, in spite of the fact that the changes of calcium retention of these patients (fig. 6) were minimal. This again indicates the possible error of placing too much emphasis on the results of blood studies in rickets, particularly on the results of determinations of calcium.

COMMENT

A study of the changes in the blood chemistry in rickets is probably not as significant as many observers have been led to believe. The results of these determinations show the content of calcium and of phosphorus in the blood at any given time, but they do not in themselves show the direction of the flow. The elements in the blood may be either excreted or retained in the body tissues. The relatively normal amount of calcium content before, during and after treatment in these cases and the significant changes in the phosphorus content made simultaneously confirm the impression of Hess and of others that the phosphorus content is much more important as a diagnostic factor in the study of rickets. There would seem to be little justification for the estimation of the calcium content and still less for considering the calcium-phosphorus product as a method of determining the presence or degree of rickets or the evidence of healing since this multiplication by an approximately normal factor merely dilutes or decreases the more important factor of the phosphorus content. A normal content of calcium ions in the blood serum of the rachitic patient has also been demonstrated. This is true regardless of the degree of activity of the rickets.[13]

The most accurate and satisfactory study for estimating the degree of rickets and the effectiveness of any type of therapy in the healing of the disease is a determination of the calcium and phosphorus balance, which shows the retention of these elements in the body, confirmed by the roentgen studies. We regret that it was not feasible for such a study to be made in more than three cases in our series. The results obtained in the cases studied are significant. In the untreated patient with rickets there was almost no retention of these bone-forming salts.

The roentgenograms of the bones of the wrists of these patients showed healing which indicated that the minerals were being deposited in the growing bones, not only in the juxta-epiphyseal portions but in the shafts as well. The patients with mild or doubtful rickets did not show definite differences in the rate of healing, but the healing was more complete, as evidenced by the roentgenograms, and the bones were more normal at the end of the experiment in the subjects to whom the intermediate and maximum amounts of irradiated yeast were fed than in the subjects given the cod liver oil supplement.

SUMMARY

From a group of eighty-three infants with clinical evidence of rickets, twenty-one subjects were selected for a three month study of the comparative antirachitic effects of irradiated dry yeast and cod liver oil. The children ranged in age from 5 to 30 months and showed rickets

13. Compere, E. L.; McLean, F. C., and Hastings, A. B.: The State of Calcium in the Blood in Rickets, J. Clin. Investigation **13**:687, 1934.

varying in severity from mild or doubtful to marked and definitely active. After division into five representative groups the first group was given a basal diet of milk, cereals, fruits and vegetables with no supplement of vitamin D. This constituted a negative control group. The second group received daily, in addition to the basal diet, 10.5 Gm. of cod liver oil made up of equal quantities of four standard brands as purchased in the Chicago retail market. The three remaining groups were given daily 0.417, 1.251 and 2.502 Gm. of irradiated dry yeast, respectively.

The change in the condition of all the subjects was noted by means of bimonthly determinations of the calcium and phosphorus content and roentgenograms of the wrists and in three cases by the determination of the mineral balance over a period of twenty days.

The findings indicated that the cod liver oil had the expected effect, both in producing a rise of the blood calcium and phosphorus levels and in stimulating the normal formation of bone. The minimum quantity of yeast, although containing very nearly the same number of rat units of vitamin D, was not so effective. Only one patient in this group showed definite improvement. On the other hand, the irradiated yeast in higher dosages was as effective an antirachitic agent as was the cod liver oil. Previous experimental data had led us to believe that the rat unit of the irradiated yeast would not be equivalent to that of cod liver oil for the use of the human infant, and accordingly the three quantities of increasing rat unitage were given. This assumption was justified by the results. By means of the calculations of the percentage of increase in the serum mineral content as reflected in the calcium-phosphorus products, and, what is much more significant, by the interpretation of the roentgenograms of the wrists, a direct comparison of these two sources of vitamin D was made. It was found that under the conditions of this experiment from 1.1 to 3.3 times as many rat units of vitamin D in the form of irradiated dry yeast as in cod liver oil was required to bring about comparable improvement in rickets in children. The yeast was easily administered, even in the maximum quantities used in these tests.

CONCLUSIONS

1. Irradiated dry yeast is an effective therapeutic antirachitic agent when given to children in sufficient quantities.

2. The minimal amount of irradiated dry yeast used in this experiment which seemed to effect a cure was 1.25 Gm. per day. This contained 6.755 International or U. S. P. revised units of vitamin D.

3. On the basis of roentgenographic evidence it was necessary to give from 1.1 to 3.3 times as many rat units of vitamin D in the form of irradiated yeast as in the form of cod liver oil to bring about a comparable degree of improvement in rickets in children.

STATE OF CALCIUM IN THE FLUIDS OF THE BODY

II. CALCIUM IN THE BLOOD IN RICKETS

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The literature and the theoretical considerations concerning the rôle of calcium in the formation of bone, and more particularly in rickets, have recently been reviewed by Peters and Van Slyke.[1] An extensive review is therefore unnecessary here. Since the work of Howland and Marriott,[2] it has been generally agreed that while the total calcium content of the serum is occasionally low in rickets such a reduction is not a consistent or a necessary factor in the pathologic physiology of this disease.

Benjamin and Hess [3] recently studied the state of calcium in normal and rachitic serums, using a combination of the methods of adsorption and ultrafiltration. They concluded that of the diffusible calcium from normal serum about two thirds is in the form of an adsorbable calcium-phosphorus complex. In rickets they found a diminution in the adsorbable fractions of calcium and an increase in the fractions designated by them as "ionic" and "protein bound." They found also that this reduction in the adsorbable fractions of calcium is intimately associated with a diminution in the total and the adsorbable fraction of phosphorus.

Two of us,[4] in studies on the state of calcium and the conditions determining its ionization in the fluids of the body, failed to confirm the conclusions of Benjamin and Hess that a large proportion of the diffusible calcium in normal serum is present in the form of an adsorb-

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A preliminary communication was published in the Proceedings of the American Society for Clinical Investigation (J. Clin. Investigation **13**:687, 1934).

From the Division of Orthopedic Surgery, Department of Surgery, the Physiological Laboratory and the Lasker Foundation for Medical Research, the University of Chicago.

1. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins Company, 1931, vol. 1, p. 830.

2. Howland, J., and Marriott, W. M.: Quart. J. Med. **11**:289 (July) 1918.

3. Benjamin, H. R., and Hess, A. F.: J. Biol. Chem. **100**:27 (March) 1933.

4. McLean, F. C., and Hastings, A. B.: J. Biol. Chem. **108**:285 (Jan.) 1935.

able calcium-phosphorus complex. Doubt, therefore, necessarily arises as to the significance of their findings in cases of rickets.

The method used by two of us (McLean and Hastings [4]) in the previous study and the discovery that a mass law relationship between calcium and protein is the chief factor in determining the ionization of calcium in normal human serum have made possible a new approach to the problem of the conditions present in rickets. The studies reported in this paper were undertaken during the course of those on the treatment of rickets by one of us (Compere) in collaboration with Porter and Roberts, published in another article.[5] This report is based on forty-seven simultaneous observations of the total protein, total calcium, ionized calcium and total inorganic phosphorus on serum from the twenty-one children studied. The diagnosis in the cases of these children varied from mild or doubtful rickets to the marked or very active form. The study included both untreated patients and patients treated for as long as one month with cod liver oil or varying amounts of irradiated yeast. Since the designations used for the patients are the same, detailed information concerning the patients and the conditions at the time of observation is available in the other paper.[5]

METHODS

As a rule, the direct observations of calcium ion concentration were made on the same samples of serum used by Compere, Porter and Roberts in their biweekly observations of the patients studied. A few observations, however, were made independently, the same methods for determination of the total calcium and total phosphorus being used. All samples of blood were taken in the morning with the patients fasting, and the serum was promptly separated from the clot.

Total nitrogen was determined by the Kjeldahl method. An arbitrary correction of 30 mg. per hundred cubic centimeters for nonprotein nitrogen was applied, and the total protein was calculated as 6.3 $\times$ (total nitrogen — nonprotein nitrogen).

The calcium ion concentration was determined by the method described by two of us.[6] The method consists essentially in comparing and matching the physiologic action of the serum with that of solutions of known calcium ion concentration, using an equal amplitude of contraction of the ventricle of the isolated heart of the frog as a criterion of equal calcium ion concentrations. The method proved to be relatively satisfactory for the examination of serum of children. Disturbing pressor effects and interference with the range of sensitivity, although present, were minimal.

A calculated calcium ion concentration was derived from the calcium-protein relationship described by two of us.[4] The calculation was based on the ionization constant of calcium proteinate from the mass law equation

$$\frac{Ca^{++} \times \text{Protein}^{=}}{\text{Calcium proteinate}} = K = 10^{-2.22}$$

5. Compere, E. L.; Porter, T. E., and Roberts, L. J.: A Clinical Comparison of the Antirachitic Value of Irradiated Yeast and Cod Liver Oil, Am. J. Dis. Child, this issue, p. 55.

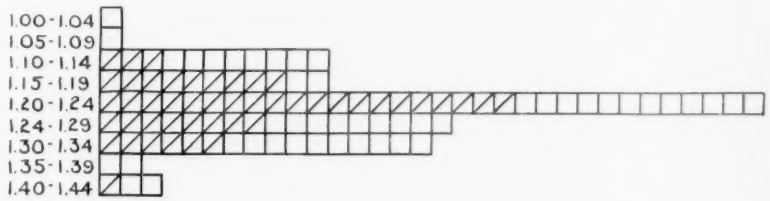
6. McLean, F. C., and Hastings, A. B.: J. Biol. Chem. **107**:337 (Oct.) 1934.

In this equation all concentrations are expressed in terms of mols per kilogram of water. Ca^{++} represents ionized calcium; calcium proteinate represents calcium bound to protein, and $Protein^{=}$ represents dissociated base-combining groups of protein, calculated as divalent ions at the p_H of the serum.

OBSERVATIONS

The values obtained from the observations were scattered in range. The fluctuations noted, being as a rule within the limits of experimental error in the methods used, are not suitable for analysis on the basis of individual cases. The results of the observations are recorded in detail in table 1.

Calcium Ion Concentration.—In the figure is illustrated the distribution of calculated and observed values for calcium ion concentration. All values fell within a range the extremes of which were 1 and 1.4 millimols per kilogram of serum water (4 and 5.6 mg. per hundred grams of serum water), the great majority falling between 1.1 and 1.35 millimols per kilogram of serum water (4.4 and 5.4 mg. per hundred grams of serum water).



Distribution of observed and calculated values for calcium ion concentration expressed in millimols per kilogram of serum water. In the chart, the hollow squares represent observed values; the squares with diagonals, the calculated values.

The mean of the observed values was 1.22 with a standard deviation of $\pm$ 0.09, and the mean of the calculated values, 1.22 with a standard deviation of $\pm$ 0.06, expressed in millimols per kilogram of serum water. The greater consistency of the calculated values may indicate a greater degree of accuracy for these values in individual cases than for those obtained by direct observation. By giving equal weight to observed and calculated values, the mean calcium ion concentration for all observations by both methods is 1.22 with a standard deviation of $\pm$ 0.08 millimols per kilogram of serum water (4.88 with a standard deviation of $\pm$ 0.32 mg. per hundred grams of serum water). This compares with a value of 1.25 with a standard deviation of $\pm$ 0.09, which was obtained similarly from a smaller number of observations on serum from a normal adult.[4] In each case it is apparent that a regulatory mechanism is operative, which maintains the calcium ion concentration in the blood within fairly narrow limits.

TABLE 1.—*Data from Observations on Serum from Twenty-One Children with a Diagnosis of Rickets* *

No.	Patient	Date, 1934	Serum Protein, per Cent	Total Calcium, Millimols per Kg.† Serum Water	Ionized Calcium, Millimols per Kg. Serum Water: Calculated Values	Ionized Calcium, Millimols per Kg. Serum Water: Observed Values	Inorganic Phosphorus, Mg. per 100 Cc.	Clinical Severity	Daily Therapy Instituted, Jan. 15, 1934
1	J. A.	2/ 5	6.58	2.63	1.20	1.25	3.16	Marked	None
		2/19	6.86	2.58	1.15	1.20	3.43		
2	L. R.	2/ 6	6.78	2.69	1.21	1.25	5.14	Moderate	None
		2/19	7.18	2.77	1.20	1.35	4.68		
3	A. W.	2/ 5	6.98	2.62	1.15	1.30	6.02	Mild	None
4	M. M.	2/ 5	6.92	2.70	1.20	1.20	4.28	Mild	None
		2/19	6.92	2.73	1.21	1.20	4.37		
5	J. T.	2/ 5	6.85	2.66	1.19	1.30	2.96	Marked	Cod liver oil, 10.5 Gm.
		2/19	6.46	2.54	1.18	1.25	3.26		
6	C. L.	2/ 5	6.34	2.67	1.25	1.20	6.56	Mild	Cod liver oil, 10.5 Gm.
		2/19	6.05	2.70	1.30	1.20	6.03		
7	J. R.	2/ 5	6.89	2.90	1.30	1.40	5.86	Moderate	Cod liver oil, 10.5 Gm.
8	An. W.	2/ 5	7.08	2.83	1.24	1.20	5.24	Very mild	Cod liver oil, 10.5 Gm.
9	J. P.	1/22	6.98	2.78	1.22	1.10	5.26	Marked	Irradiated yeast, 0.417 Gm.
		2/ 5	7.25	2.76	1.19	1.20	5.38		
		2/19	6.86	2.71	1.20	1.35	5.18		
10	F. T.	2/ 5	6.53	2.78	1.28	1.25	5.80	Moderate	Irradiated yeast, 0.417 Gm.
		2/19	6.55	2.67	1.22	1.20	4.65		
11	J. H.	1/ 8	6.71	2.44	1.10	1.20	4.96	Mild	Irradiated yeast, 0.417 Gm.
		1/22	7.33	2.88	1.24	1.00	3.50		
		2/ 5	6.79	2.80	1.28	1.30	4.72		
		2/19	6.73	2.54	1.15	1.20	5.08		
12	D. F.	1/22	7.53	2.71	1.13	1.10	4.72	Very mild	Irradiated yeast, 0.417 Gm.
		2/ 5	6.66	2.71	1.23	1.10	5.40		
		2/19	7.43	2.80	1.18	1.25	5.16		
13	Je. T.	1/22	7.27	2.90	1.25	1.10	3.38	Marked	Irradiated yeast, 1.251 Gm.
		2/ 5	6.98	2.74	1.20	1.30	6.34		
		2/19	6.32	2.95	1.40	1.25	5.48		
14	F. Y.	1/22	6.53	2.86	1.32	1.05	6.08	Moderate	Irradiated yeast, 1.251 Gm.
		2/ 5	6.35	2.59	1.21	1.20	6.74		
		2/19	6.45	2.55	1.19	1.30	5.20		
15	J. B.	2/ 5	6.73	2.77	1.26	1.30	6.18	Mild	Irradiated yeast, 1.251 Gm.
16	F. M.	2/ 5	6.33	2.63	1.23	1.25	5.84	Very mild	Irradiated yeast, 1.251 Gm.
		2/19	6.80	2.68	1.20	1.30	5.54		
17	R. M.	1/22	6.20	2.56	1.21	1.10	3.52	Marked	Irradiated yeast, 1.251 Gm.
		2/ 5	5.89	2.39	1.17	1.15	6.44		
		2/19	5.78	2.45	1.20	1.25	5.53		
18	Y. W.	1/22	6.35	2.62	1.22	1.10	4.56	Moderate	Irradiated yeast, 2.502 Gm.
		2/ 5	7.33	2.63	1.11	1.20	5.42		
		2/19	6.63	2.66	1.21	1.25	4.96		
19	O. H.	2/ 5	6.73	2.77	1.26	1.30	6.18	Moderate	Irradiated yeast, 2.502 Gm.
		2/19	5.99	2.59	1.26	1.40	4.43		
20	V. W.	2/ 5	5.97	2.47	1.20	1.10	5.38	Very mild	Irradiated yeast, 2.502 Gm.
		2/19	6.57	2.86	1.30	1.30	6.44		
21	E. C.	1/22	6.83	2.90	1.30	1.15	4.84	Mild	Irradiated yeast, 2.502 Gm.
		2/ 5	6.04	2.62	1.26	1.10	5.62		
		2/19	6.08	2.68	1.30	1.35	5.55		

* The numbers and designations of patients are identical with those in the study of Compere, Porter and Roberts.[5]

† Millimols per Kg. serum water = Mols $\times 10^3 = \frac{\text{Mg. per 100 Gm. of serum water}}{4}$

The maximum deviation between the observed and the calculated value for calcium ions is 0.27 millimols and the average deviation ± 0.08 millimols. The combination of possible errors in each method of arriving at the calcium ion concentration, together with the fact that all observations were within a comparatively narrow range of values for total calcium and total protein, leads to the expectation of a rather low degree of correlation between the observed and the calculated value. Calculation of the correlation coefficient gives a value of + 0.476 with a prob-

TABLE 2.—*Observations from Table 1 Grouped for Purposes of Comparison*

	Number of Observations	Mean Value of Serum Protein, per Cent	Mean Value of Total Calcium, Millimols per Kg. Serum Water	Ionized Calcium, Millimols per Kg. Serum Water				Mean Value of Inorganic Phosphorus, Mg. per 100 Cc.
				Calculated Values		Observed Values		
				Mean	Standard Deviation	Mean	Standard Deviation	
Total number of patients	47	6.67	2.69	1.22	±0.06	1.22	±0.09	5.12
Grouped by phosphate concentration								
Phosphates < 4.25 mg. per 100 cc.	7	6.79	2.68	1.20	±0.04	1.17	±0.10	3.31
Phosphates 4.25 to 5.24 mg. per 100 cc.	17	6.81	2.69	1.21	±0.05	1.24	±0.08	4.83
Phosphates > 5.24 mg. per 100 cc.	23	6.53	2.70	1.24	±0.06	1.22	±0.09	5.87
Grouped by clinical classification								
Marked rickets	13	6.64	2.66	1.21	±0.06	1.22	±0.08	4.56
Moderate rickets	13	6.64	2.70	1.23	±0.05	1.25	±0.10	5.36
Mild rickets	13	6.65	2.70	1.23	±0.06	1.21	±0.09	5.21
Very mild (doubtful) rickets	8	6.79	2.71	1.21	±0.05	1.20	±0.08	5.46
Grouped by type of treatment								
Untreated	8	6.87	2.64	1.18	±0.04	1.24	±0.05	4.50
Irradiated yeast, 0.417 Gm. daily	11	6.97	2.74	1.21	±0.05	1.19	±0.10	4.99
Irradiated yeast, 1,251 Gm. daily	12	6.47	2.67	1.24	±0.06	1.21	±0.09	5.52
Irradiated yeast, 2.502 Gm. daily	10	6.45	2.68	1.24	±0.06	1.22	±0.11	5.34
Cod liver oil, 10.5 Gm. daily	6	6.61	2.72	1.24	±0.05	1.26	±0.07	4.98
All treated patients	39	6.63	2.70	1.23	±0.06	1.22	±0.10	5.24

able error of ± 0.076. The mass law equation and its constant used in arriving at the calculated calcium ion concentrations were based on observations extending over a wider range and yielding a correlation coefficient of + 0.981 with a probable error of ± 0.005.[4]

The conclusion to be drawn from these observations is that in this series of children the calcium ion concentrations did not differ significantly, either in the mean concentration or in the range of variation, from those in adults without evident calcium dyscrasia.

The findings as recorded in the figure are therefore indistinguishable from those obtained on normal human serum. An attempt was

made, however, to determine whether a correlation between the severity of the rachitic process and the findings with reference to the state of calcium could be demonstrated, the observations in mild or doubtful cases serving as controls. Separation of the observations into groups, on the basis of the concentration of inorganic phosphorus, of the clinical classification relative to the severity of the disease process and the presence or absence of treatment, however, failed to reveal such a correlation (table 2), all the fluctuations being within the limits of experimental error.

The failure to record an increase in calcium ion concentrations in the serum of treated patients should not, however, be interpreted as evidence against the ability of viosterol to produce such a change, since the studies were neither planned with this aim in view nor carried out long enough with the patients under treatment to permit a conclusion.

These findings indicate again that there is no quantitatively significant change in the state of calcium in the blood in rickets. Moreover, the agreement between calculated and observed values for calcium ion concentration, within the limits of experimental error, indicates that in the serum of children with rickets, as well as in normal human serum, there is no necessity for postulating quantitatively significant amounts of a bound but diffusible form of calcium.

COMMENT

Previous experience has shown that the level of total calcium in the serum is not necessarily changed in rickets.[1] To this is added the evidence from this study that the state of the calcium in the serum of patients with rickets is not altered to an extent discoverable by the methods used. It appears, therefore, that the pathologic state observed in rickets is not to be explained on the basis of a change in the amount or state of the calcium in the blood stream.

Against this conclusion are the findings of Benjamin and Hess[3] already referred to. It appears that their observations can be reconciled with ours only on the basis of the assumption that the adsorbable calcium-phosphorus complex which they described is not preformed in the serum in significant amounts but that, in the presence of bicarbonate and the adsorbing agent used (barium sulphate), formation and adsorption of such a complex do occur. Benjamin[7] has shown that in "artificial ultrafiltrates" the same phenomenon of adsorption occurs and that, as in the case of ultrafiltrates from serum, the adsorption of calcium, with the concentrations of calcium and bicarbonate constant, is directly correlated with the concentration of phosphorus. It appears, therefore, that the results of Benjamin and Hess are dependent in some way on

7. Benjamin, H. R.: J. Biol. Chem. **100**:57 (March) 1933.

the reduction of the concentration of inorganic phosphate in rachitic serum but that they do not necessarily reflect any other change characteristic of rickets.

CONCLUSIONS

Neither the amount nor the state of calcium in the serum of blood from rachitic children is necessarily altered from that of normal serum.

In a series of forty-seven observations on the serum from children with a condition diagnosed as rickets varying from very mild or doubtful to marked or very active, the calcium ion concentration has been found to vary from 1 to 1.4 millimols per kilogram of serum water, with a mean of 1.22 and a standard deviation of ± 0.08. This value corresponds closely with previous findings in the serum of the normal adult.

HEMATOGENOUS TUBERCULOSIS IN CHILDREN

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Knowledge of the pathogenesis of primary tuberculous infection in childhood has been increasing by leaps and bounds in the last fifteen years. And with this has come a revolution in the conception of the part that the blood stream plays in the postprimary development of tuberculosis.

Originally dissemination by the blood stream was conceived of as an occasional, much dreaded, invariably fatal accident, the main pathologic feature of which consisted of tubercles of miliary size scattered throughout the body or rarely localized to the meninges or lungs.

With the newer knowledge that in probably all cases of primary tuberculosis a few bacilli at least find their way into the blood, there is introduced a different conception of the part that the blood stream plays, and on the basis of clinical and pathologic observations many facts can be interpreted which heretofore have seemed obscure.

The conception of tuberculosis as a systemic disease the point of origin of which is usually in the lungs has been recognized for years in the French literature and is also generally accepted by an increasing number of German workers on tuberculosis. Interest has been especially stimulated by the work of Liebermeister in actually finding tubercle bacilli in the blood in various types of tuberculosis.

Proof that bacilli find their way into the blood stream is based on pathologic and clinical facts. Liebermeister [1] showed that bacilli may be found by cultures of the blood or by injection of blood into guinea-pigs in a large percentage of cases of "open" tuberculosis, often in cases of "closed" tuberculosis and in some cases in which the patient is under observation for tuberculosis without showing abnormal physical signs. The work of Lowenstein, who claimed similar results obtained by culturing tubercle bacilli from the blood, has been questioned because of the high percentage of cases in which the bacilli were found and the many disorders, especially those of a vague rheumatic nature without known relation to tuberculosis, in which tubercle bacilli were cultured from the

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1. Liebermeister, G.: Studien über Komplikationen der Lungentuberkulose und über die Verbreitung der Tuberkelbazillen in Organen und im Blut der Phthisiker, Virchows Arch. f. path. Anat. **197**:332, 1909; Die Bazillaemie, in Engel, S., and von Pirquet, C.: Handbuch der Kindertuberkulose, Leipzig, Georg Thieme, 1930, vol. 1, p. 451.

blood stream. Moreover, while a few workers have confirmed his observations, the majority have been unable to do so. Liebermeister himself obtained many negative cultures of the blood in cases of miliary tuberculosis, which is universally accepted to be the result of dissemination by the blood stream. He expressed the belief that his failure to culture tubercle bacilli or to find them by the inoculation of guinea-pigs in these cases was due to limitations in technic, and it is certainly within the realm of possibility that this cause prevented other workers from confirming his positive results. Moreover, there are probably certain phases of the disease, just as there are of meningococcic meningitis or of pneumonia, in which it is relatively easy to find organisms in the blood and others in which sterile cultures result. For instance, Grethmann [2] injected bacilli obtained from the blood of six selected patients revealing protracted hematogenous dissemination into twenty-four guinea-pigs, all of which died of tuberculosis. The actual number of bacilli present in the blood stream, moreover, is probably usually small. Liebermeister found only occasionally a few bacilli in 2 cc. of blood, and, so far as is known, no increase in the number of bacilli takes place while they are circulating in the blood. Moreover, inoculation of guinea-pigs is not a delicate method for the finding of bacilli. It has been shown experimentally that 10 bacilli is the smallest dose which is infective for a guinea-pig, although Selter claimed to have infected guinea-pigs with as few as 2 bacilli. In other words, bacteriologic proof exists that tubercle bacilli circulate at times in the blood stream of tuberculous persons, but the technic for demonstrating them is so far from perfect that the percentage of cases in which they may be found and the number of bacilli are uncertain.

The next question with which one is concerned is the mechanism by which the bacilli reach the blood. It has been clearly established by Ghon and others that in 95 per cent of all cases of first tuberculous infection the primary focus is situated in the lungs, usually just under the pleura. Almost as soon as the primary focus begins to form, tubercle bacilli find their way to the regional lymph nodes, and Ghon, Kudlich and Schmiedl [3] have shown by the study of serial sections the manner in which tuberculous infection passes through the tracheobronchial and paratracheal lymph nodes to the lymphatic duct and so into the venous circulation. This, then, is one of the methods by which bacilli reach the blood stream, and it is probably true that a few bacilli at least are carried by this route in every case of first tuberculous infection. These tubercle bacilli create hematogenous metastases, which are

2. Grethmann, W.: Personal communication.

3. Ghon, A.; Kudlich, H., and Schmiedl, S.: Die Veränderungen der Lymphknoten in den Venenwinkeln bei Tuberkulose und ihre Bedeutung, Ztschr. f. Tuberk. **46**:1 and 97, 1926.

most likely to be in the apexes of the lungs and in the spleen but which frequently also invade the bones and joints. The resultant tubercles are generally of miliary size, but the lesions may be relatively few in number. The picture is not necessarily the familiar one of acute generalized miliary tuberculosis, which is the result of a single hematogenous dissemination of a large number of bacilli. This condition is more often produced either through erosion of the wall of a blood vessel by a caseating focus of tuberculosis or by dissemination from a so-called "intimal" tubercle. Weigert [4] first described direct invasion of the blood stream, and it has been demonstrated repeatedly by the evidence of gross and histologic examination. Moreover, it can be postulated, as Loeschke [5] pointed out, whenever hemorrhage into a caseous focus or lymph node is seen. Because primary hemorrhage into a tuberculous lymph node practically never occurs, it may usually be correctly inferred that the extravasated blood comes from the break in the wall of the vessel, owing to erosion by the caseating tuberculous focus. My associates and I have seen hemorrhages into nodes several times during autopsies performed on patients dying of generalized tuberculosis.

Secondary invasion of the blood stream occurs when an intimal tubercle discharges a large number of bacilli into the blood at one time after having remained inactive for an uncertain period. Such a tubercle, which is most commonly seen at the junction of small pulmonary veins, may arise when a few bacilli circulating in the blood are caught in the eddy at a bend or fork in the blood vessel and, owing in part to the slowing of the current and in part to little understood changes which perhaps render the lining of the blood vessel more susceptible to invasion, the bacilli enter the intima and proliferate there.

The work of Rich [6] is interesting and important in the consideration of the pathologic changes in hematogenous tuberculosis. In more than 90 per cent of his cases of tuberculous meningitis he observed an older caseating tuberculous lesion in the brain, and he expressed the belief that the invasion of the meninges is due to the rupture of this focus and not directly to the tubercle bacilli circulating in the blood as part of an acute generalized dissemination.

Of course it is obvious that not every tubercle bacillus that enters the blood stream necessarily results in the formation of a tubercle. Variations in susceptibility and in local immunity must play a large part. A number of nonspecific factors, such as the occurrence of measles, may

4. Weigert, Carl: Ueber Venentuberkel und ihre Beziehungen zur tuberkulösen Blutinfection, Virchows Arch. f. path. Anat. **88**:307 (May) 1882.

5. Loeschke, H.: Die haematogene Tuberkulose, Beitr. z. Klin. d. Tuberk. **81**:171, 1932.

6. Rich, A. R., and McCordock, H. A.: The Pathogenesis of Tuberculous Meningitis, Bull. Johns Hopkins Hosp. **52**:5 (Jan.) 1933.

alter susceptibility and pave the way for the clinical evidence of hematogenous extension. There may well be constitutional, individual and inherited variations. There are undoubted variations in the susceptibility of the organs. The stomach and pancreas are relatively immune, but tubercles are frequently noted in the spleen. The seasonal variations in the occurrence of tuberculous meningitis are well known. But probably the greatest factors which determine the outcome in a case of bacillemia are the number of bacilli and the amount of toxins which are released into the blood stream.

The variety in the clinical picture thus seems to be dependent on three main features: the dosage of tubercle bacilli conveyed to the blood stream; the frequency of repetition of this means of dissemination, and, lastly, the uncertain factors of allergy and the relative immunity of the body to the dosage received. There is no reason to adhere to the belief that a single dose of bacilli may enter the blood stream but that repeated doses do not occur. It has been established, both clinically and pathologically, that protracted dissemination by way of the blood stream actually takes place. The resulting pathologic picture has been recognized in part for many years. Schürmann [7] first used the term protracted progressive dissemination. Recently Grethmann made a careful study of this form of tuberculosis, in which he added pathologic evidence and stressed the clinical features.

Ranke's [8] classification of tuberculosis, while imperfect, is helpful in the interpretation of clinical observations. He postulated a first stage of the primary complex, in which the bacilli travel by the lymphatics; a second stage, or stage of generalization, in which the spread of the disease occurs chiefly by the lymphatics and blood stream, although all avenues of dissemination may be utilized, and a third stage, in which the disease is again localized to one or more principal areas, the stage of chronic phthisis. In this stage the spread is chiefly by direct extension or by intracanalicular dissemination, that is, by way of existing channels, such as the bronchi, gastro-intestinal tract, ureters, etc. Ranke thought that in persons of the white race the second stage was often omitted or was insignificant. Evidence, however, indicates that in this respect he was wrong, and, as has already been shown, it is probable that the invasion of the blood stream follows closely a primary tuberculous infection as a practically universal phenomenon.

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7. Schürmann, P.: Ueber einige Besonderheiten im anatomischen Bild der Tuberkulose bei protahierter progressiver Durchseuchung, Beitr. z. Klin. d. Tuberk. **62**:591, 1926.

8. Ranke, K.: Primaeraffekt, sekundaere und tertiaere Stadien der Lungentuberkulose auf Grund von histologischen Untersuchungen der Lymphknoten der Lungenpforte, Deutsches Arch. f. klin. Med. **119**:297, 1916.

Four main groups of cases of tuberculous infection due to hematogenous dissemination can be distinguished clinically: (1) the cases of the protracted form of generalized dissemination, which when marked is a clinical entity; (2) the easily recognized cases of acute generalized miliary tuberculosis; (3) cases in which, as in those of renal or osseous tuberculosis, or tuberculosis of the bones, the predominant lesion is of hematogenous origin but is not usually thought of in those terms, and (4) cases in which bacillemia may not be evident and in which there may be no changes evident on physical examination. The end-result in the occult cases of bacillemia may often be recognized by roentgen examination of the lungs or, more rarely, of the spleen and cervical nodes.

The clinical picture which results from marked protracted hematogenous dissemination of tubercle bacilli is a cleancut entity, and once it is recognized the diagnosis of the condition can usually be made in all degrees of severity. I made the diagnosis in my first case after seeing Dr. Grethmann demonstrate autopsy specimens obtained from an adult, and since that time this lesion has been diagnosed many times and verified by autopsy.

The most characteristic lesions of this form of tuberculosis at the height of its development are marked panadenitis and panserositis and associated roentgenographic evidence in the lungs of bilateral, symmetrically distributed nodules, varying from submiliary tubercles to those the size of a half dollar, and of similar lesions in the spleen and other organs. Sometimes the involvement of the serous surfaces is limited to clear exudates or to extensive adhesions. In the marked cases caseation of the serous surface may be present. The tracheobronchial as well as the superficial nodes are tremendously enlarged. A mass of inguinal nodes producing elephantiasis of the leg as a result of occlusion of the lymphatics has been seen. Sometimes there are other clinical evidences of hematogenous tuberculosis. Many of my patients showed involvement of the joints.

Sometimes the origin of the picture is emphasized, and the time of the dissemination of the bacilli by the blood stream is actually demonstrated by the appearance at intervals of crops of papulonecrotic tuberculids. With these lesions are often associated enlargement of the spleen and sometimes that of the liver, swelling of the superficial lymph nodes and sometimes acute exudative reaction around a preexisting focus of tuberculosis, such as occurred in one case in which a tuberculous knee suddenly became more swollen, reddened, hot and tender. This condition acted exactly as such lesions do after a subcutaneous dose of tuberculin, subsiding within forty-eight hours. More often, similar exudative lesions appear in the lungs, simulating pneumonia, or they may occur without physical signs but with the roentgenographic appearance of an infiltration. Transient attacks of meningeal or cortical irritation

with a variety of neurologic signs simulating those of tuberculous meningitis occur in almost every case. Changes in the pressure of the spinal fluid and increase in the number of cells and in the globulin content may take place, but chemical changes have not been observed nor have tubercle bacilli been found in the spinal fluid. On pathologic examination small, caseating foci in the meninges or cortex are often seen, and in one case adhesions between the hemispheres resulting from preexisting meningitis were noted.

The lesions in the lungs at first are usually without abnormal physical signs, and even in marked cases they may continue in a silent state for months or even for years. Usually the lesions become caseated and may coalesce, and the picture is complicated by lymphatic and bronchogenic extension, so that eventually it may be impossible to distinguish it from that of chronic ulcerative tuberculosis with bronchiogenic dissemination. This is especially true in the cases in which pulmonary nodules of hematogenous origin in the lower lobes have tended to heal and become absorbed and progression has been limited largely to the upper parts of the lungs. Rarely in children is clinical evidence found of the thin-walled cavity which is described as one of the characteristic features of hematogenous pulmonary tuberculosis in adults,[9] although pathologic evidence of small cavities of this type may be observed.

REPORT OF CASES

The following case (figs. 1, 2 and 3) represents the form of protracted generalized dissemination in which the disease is subacute and rapidly fatal.

CASE 1.—F. I., a Negro 9 years old, was admitted to the hospital on Oct. 5, 1931, and died twenty-three days later. He had never been ill before he had "pneumonia" in June 1931. Fever, cough and increasing weakness followed this illness. He was emaciated and acutely ill with enlargement of all the superficial nodes, a large mass of inguinal nodes and marked swelling of the right leg. Dulness, diminished breath sounds and consonating râles were present throughout the upper lobe of the right lung, with bronchial breath sounds at the angle of the scapula and inconstant, moist râles in the remainder of both lungs. The abdomen was full and tense; the liver and spleen were apparently enlarged. A hemorrhage from the intestinal tract occurred ten days after his admission.

Anatomic Diagnosis.—The autopsy (Dr. Grethmann) revealed a tuberculous primary complex in the lungs with extensive tuberculous adenitis and lymphangitis of the bronchopulmonary, tracheobronchial and paratracheal nodes; hematogenous dissemination of miliary and conglomerate tubercles throughout the lungs, spleen, liver, kidneys and meninges; tuberculous panadenitis and panserositis (pleura, pericardium, meninges and peritoneum); ulcerated pulmonary tuberculosis with

9. Miller, J. A.: Haematogenous Pulmonary Tuberculosis, Am. Rev. Tuberc. **29**:489 (May) 1934.

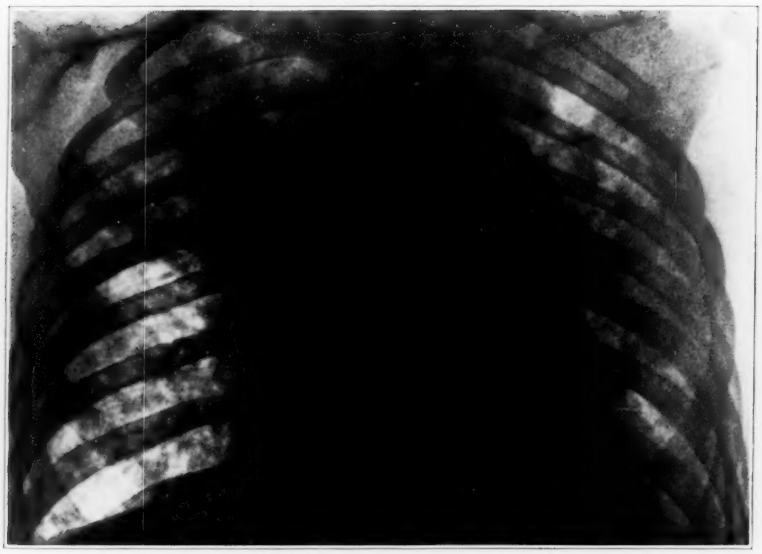

Fig. 1 (case 1).—Roentgenogram of the lungs, showing extensive involvement of both pulmonary fields and widened mediastinum in a patient with relatively few physical signs.

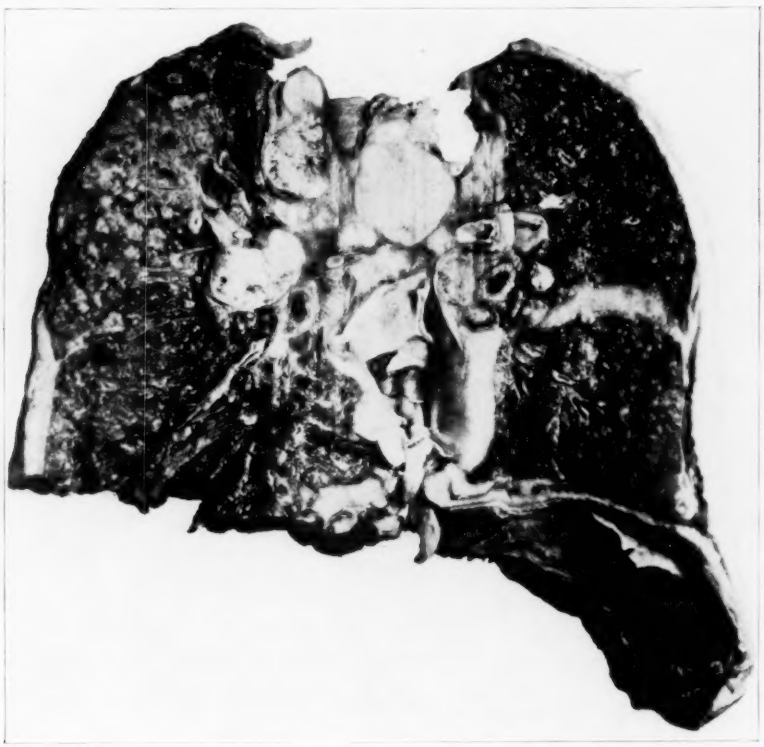

Fig. 2 (case 1).—Cut surface of the organs of the chest, showing caseous pleuritis and peritonitis; caseous lymphadenitis and lymphangitis of the broncho-pulmonary, tracheobronchial and mediastinal lymph nodes, and hematogenous foci of varying sizes with superimposed bronchogenic foci.

intracanalicular dissemination into the lungs and the intestinal tract, and ulcerated tuberculosis of the cecum and colon.

The next case represents the chronic type of protracted hematogenous dissemination which, if seen only in the final stages, may be difficult or impossible to recognize clinically.

CASE 2.—T. D., a white boy 8 years old, had a history of contact with a tuberculous member of his family. At 3 years of age enucleation of the eye had been performed because of the possibility of tuberculoma. A roentgenogram of the lungs taken eighteen months later showed miliary tuberculosis (fig. 4 *A*). The child was in fair general condition and presented no abnormal signs in the lungs. Two years later a roentgenogram of the chest showed progression of the lesion, which was largely in the upper lobes (fig. 4 *B*), but still there were no symptoms or abnormal physical signs. A short time after this examination the child had pertussis, and soon the hematogenous pulmonary lesions began to break down.

Fig. 3 (case 1).—Cut surface of the spleen, showing varying sizes of caseous foci of hematogenous origin.

Physical examination of the lungs as well as the roentgenograms gradually disclosed a picture indistinguishable from that of chronic ulcerative tuberculosis of the lungs (fig. 4 *C*). The patient died at 8 years of age of bilateral, caseous renal tuberculosis, but the autopsy gave evidence of the hematogenous origin.

In still another type the course of the disease is chronic, but the outstanding lesions remain clearly of hematogenous origin. In such cases one is more likely to note pathologic evidence of the fibrotic changes in the surrounding pulmonary tissue which occur more commonly in adults than in children with protracted hematogenous dissemination.

CASE 3.—V. C., a Negro girl 10 years old, was admitted to the hospital in December 1932. She had undergone operation for tuberculosis of the right knee

three years before her admission. Enlargement of the lymph nodes in the cervical and inguinal regions was noted at about the same time. She had had chronic purulent otitis media for more than two years. On examination the child showed marked malnutrition, general enlargement of the superficial lymph nodes, a chronically discharging right ear and an enlarged, distended abdomen. The heart was

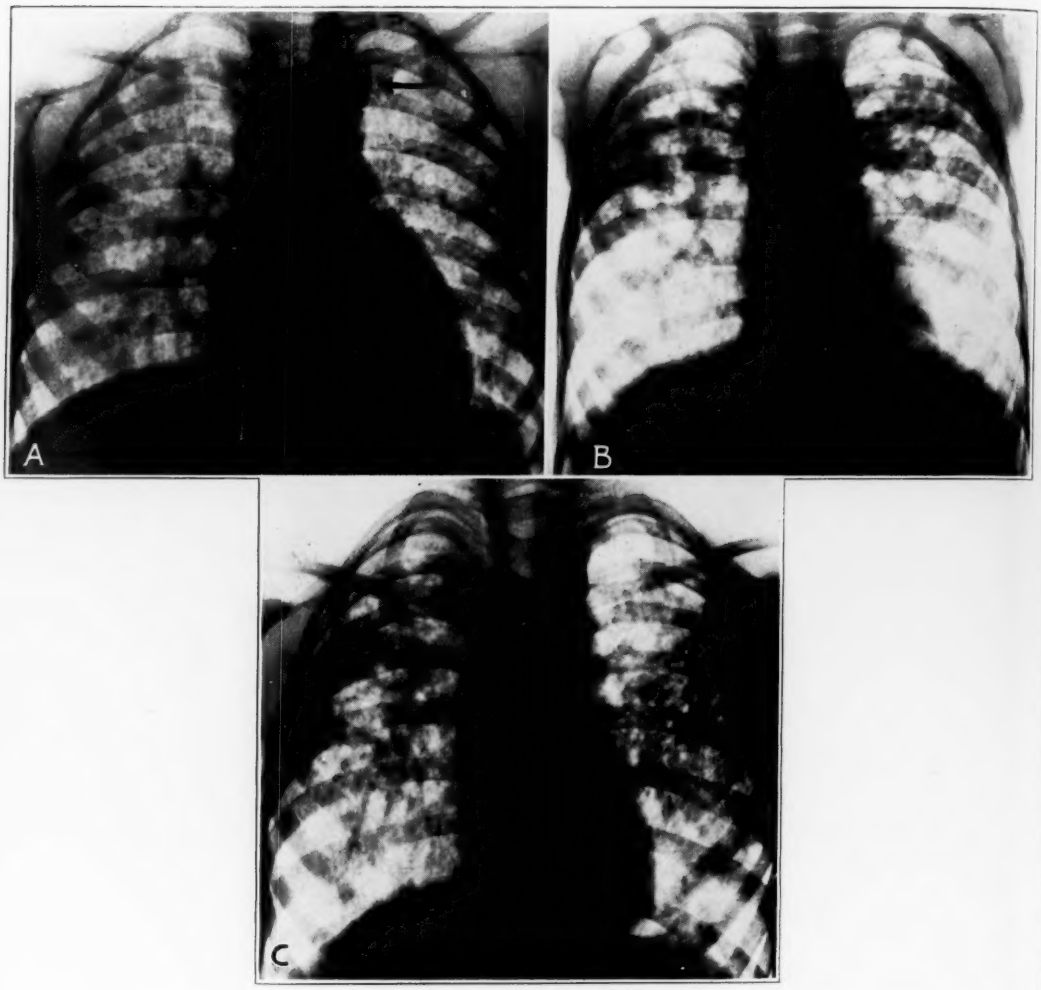

Fig. 4 (case 2).—Roentgenograms of the lungs. *A*, taken in 1928, shows miliary tuberculosis in the lungs and the calcified node in the paratracheal region of the left side which is part of the primary complex. *B*, taken in 1930, shows that the pulmonary foci have largely disappeared in the lower lobes and that the lesions have progressed in the upper portions of both pulmonary fields. *C*, taken in 1932, shows chronic ulcerative pulmonary tuberculosis with cavitation and bronchogenic extension, the end-result of hematogenous dissemination.

enlarged, but the sounds were of normal quality; dulness and diminished breath sounds were present at the base of the right lung adjacent to the spine, and incon-

stant moist râles of medium intensity were heard over the entire right lung. Roentgen examination of the lungs revealed a typical picture of protracted hematogenous dissemination (fig. 5 *A*).

During the next six months the patient showed progressive evidence of a destructive lesion of the lungs and increasing râles on both sides. In May 1933 she became acutely ill with high fever, signs of consolidation throughout the upper lobes of the right lung, increase in the size of the superficial lymph nodes and a marked increase in the swelling of the right knee joint, which became painful and hot. The acute symptoms subsided within a few days, but the exudative infiltration in the lungs gave roentgenographic evidence of clearing only after three months. The general condition became progressively worse; the temperature was elevated daily, and tubercle bacilli were found in the sputum. In December 1933 the child had a persistent high fever of irregular course and consonating râles throughout both lungs. It was difficult to distinguish the roentgenographic picture from that of chronic ulcerative pulmonary tuberculosis (fig. 5 *B*).

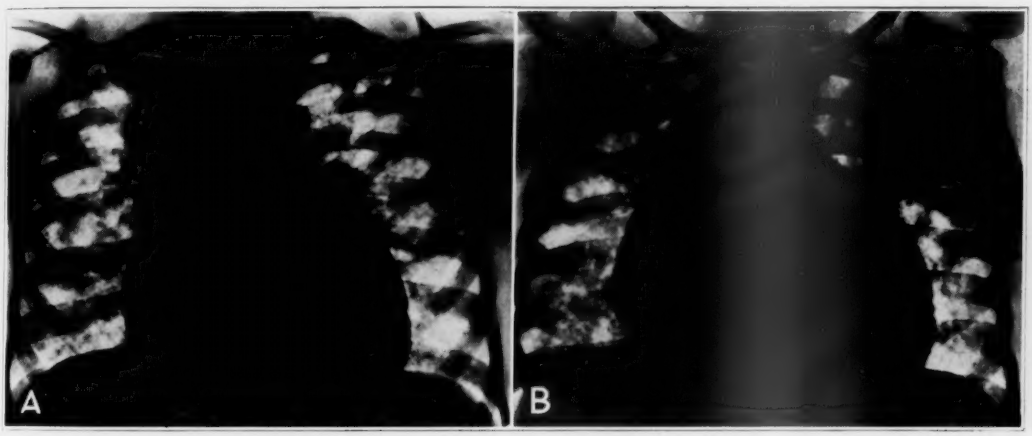

Fig. 5 (case 3).—*A* is a roentgenogram of the lungs taken at the time of admission, showing the widening of the mediastinum and the diffusely distributed foci of varying size throughout both pulmonary fields; *B*, a roentgenogram of the lungs taken one year after that shown in figure 5 *A*, revealing confluence of the hematogenous lesions and increased evidence of bronchogenic extension at the bases of both lungs, especially on the right side.

The patient died early in 1934.

Autopsy (by Dr. Grethmann) revealed a caseous primary focus with a hyalinized capsule in the lower lobe of the right lung (fig. 6); caseous tuberculous involvement of the bronchopulmonary, tracheobronchial and paratracheal lymph nodes as well as of the cervical, axillary, mesenteric, retroperitoneal and parapancreatic lymph nodes; ulceration extending into the lower pole of the thyroid gland and into the pancreas; diffuse nodular fibrosis of both lungs; ulcerative tuberculosis with cavitation in the upper lobes of both lungs; ulcerative and caseous endobronchitis resulting from bronchogenic dissemination, with caseating bronchopneumonia in the more dependent parts of the lungs (fig. 6); serofibrinous pleurisy of both lungs; hematogenous metastatic tuberculosis of the spleen; tuberculous ulcerative enteritis of recent development, undoubtedly the result of swallowed

sputum; caseous ulcerative tuberculosis of the right middle ear, and tuberculous meningitis of the right parietal lobe.

Occasionally a child is seen who has an undoubted case of protracted hematogenous dissemination but who after a time shows no clinical evidence of progression and later presents evidence of retrogressive lesions. This variation, I think, may be dependent on the dosage and

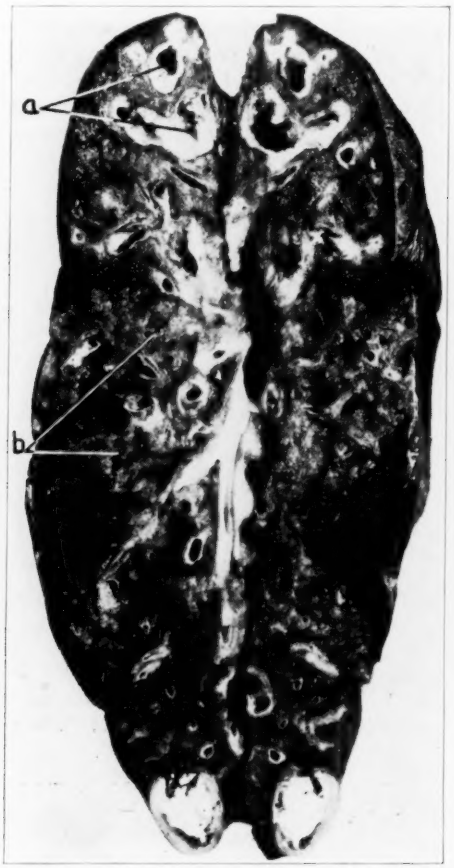

Fig. 6 (case 3).—Cut surface of the right lung, showing the primary tuberculous focus with hyalinized capsule at the base of the lower lobe, ulcerative tuberculous endobronchitis in the apex (*a*), tuberculous bronchopneumonia in the upper and middle lobes (*b*), fine-grained bronchogenic dissemination in the middle lobe and the upper part of the lower lobe and diffuse nodular fibrosis, the end-result of preexisting hematogenous tuberculosis.

character of the disseminated material and possibly also on alterations in the tissue reactions.

Case 4.—C. W., a Negro, was admitted to the wards at 2 years of age with the diagnosis of generalized miliary tuberculosis. He was in an excellent state

of nutrition (fig. 7) and had a normal temperature. His disease had been discovered by chance. A roentgenogram of the lungs revealed innumerable shadows of miliary size throughout both pulmonary fields and a large mass of tracheobronchial and paratracheal nodes on the right side (fig. 8*A*). Physical examination of the lungs gave normal findings. The spleen was enlarged and could be distinctly felt several fingerbreadths below the costal margin. All the superficial lymph nodes were enlarged and discrete but were not tender. For five months the child had successive crops of papulonecrotic tuberculids, the appearance of which was accompanied by an increase in the size of the superficial lymph nodes and spleen but not by fever. After a period of subsidence of these signs, the cycle would again begin. The intracutaneous tuberculin test gave positive results with 0.01 mg. Several times diffuse shadows were seen in the roentgenogram of the lungs which were

Fig. 7 (case 4).—Photograph of the patient taken in December 1931, showing the excellent nutritional state.

interpreted as due to exudative infiltrations. These shadows appeared suddenly and gradually disappeared. During one of these periods the child showed signs of meningeal irritation which it was at first thought would develop into tuberculous meningitis. Gradually the nodules in the lungs became less distinct; calcifications appeared in the paratracheal nodes and in the parenchyma (fig. 8*B*), and sixteen months after his admission definite calcifications in the spleen were first observed (fig. 9). Six months later he died of acute pericarditis, and to the great amazement of the observers relatively little evidence of the caseous hematogenous lesions could be seen in the lungs.

Autopsy (by Dr. Grethmann) revealed a calcified tuberculous primary focus in the lower lobe of the right lung with calcified bronchopulmonary and tracheobronchial lymph nodes; calcified and caseous paratracheal lymph nodes on the

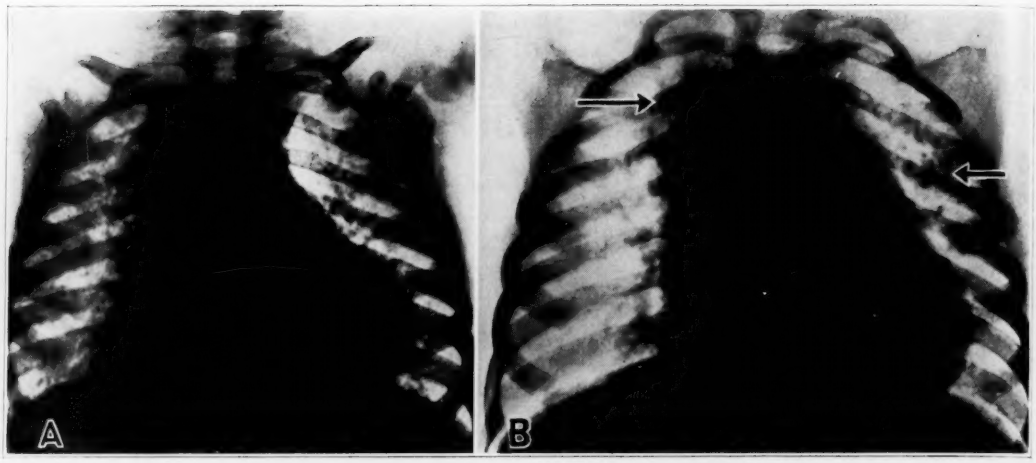

Fig. 8 (case 4).—*A* is a roentgenogram of the lungs taken in December 1931, showing foci of miliary size scattered throughout both pulmonary fields and enlargement of the tracheobronchial and paratracheal lymph nodes on the right side; *B*, roentgenogram taken in May 1933, showing calcification of the paratracheal nodes in the upper part of the mediastinum on the right side and deposits of calcium in the upper part of the field of the left lung.

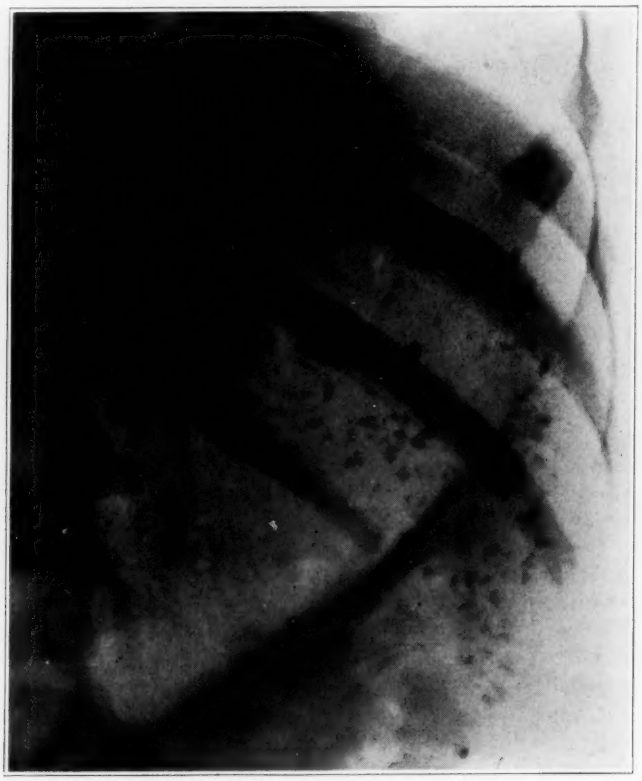

Fig. 9 (case 4).—Roentgenogram taken in May 1933, showing calcifications in the spleen.

right side (fig. 10) with ulceration into the upper lobe of the right lung and formation of cavities and tuberculous aspiration bronchopneumonia of the upper lobe of the right lung; chronic hematogenous metastatic tuberculosis of the lungs, liver, spleen (fig. 11) and meninges in different stages of progression and regression with the formation of tubercles, fibrosis and calcification; collateral emphysema in both lungs; miliary tuberculosis of the kidneys; ulcerative tuberculosis of the cortex of the right kidney; calcified and caseous tuberculosis of the deep right cervical, mesenteric and retroperitoneal lymph nodes, and chronic adhesive pleuritis, pericarditis, peritonitis, perisplenitis and meningitis.

Fig. 10 (case 4).—Cut surface of the right lung, showing chronic adhesive pleuritis, caseous and calcified tuberculous adenitis of the paratracheal lymph nodes on the right side and the residue of hematogenous as well as of bronchogenic foci throughout the lung.

The second clinical type, acute generalized hematogenous dissemination, is due to the entrance of a single dose of tubercle bacilli into the blood stream, producing tubercles of miliary size throughout the body. This is the classic picture which first occurs to every mind when hematogenous tuberculosis is mentioned. It is known that this type is usually

fatal, but occasionally healing takes place. No illustrations of this form are given in this report, as the clinical and anatomic pictures are so universally recognized.

The third group of cases is also easily recognized clinically, but it is one which physicians have not necessarily trained themselves to regard as the result of dissemination by the blood stream. In this group are included practically all the extrapulmonary forms of tuberculosis which are seen in childhood—for example, the cases of "scrofula" occurring in children with tuberculosis of one or more groups of superficial nodes and associated often with tuberculous infections of the bones or joints and not infrequently with tuberculous lesions of the skin or eyes. Depending on the stage in which the patients are seen, evidence of a

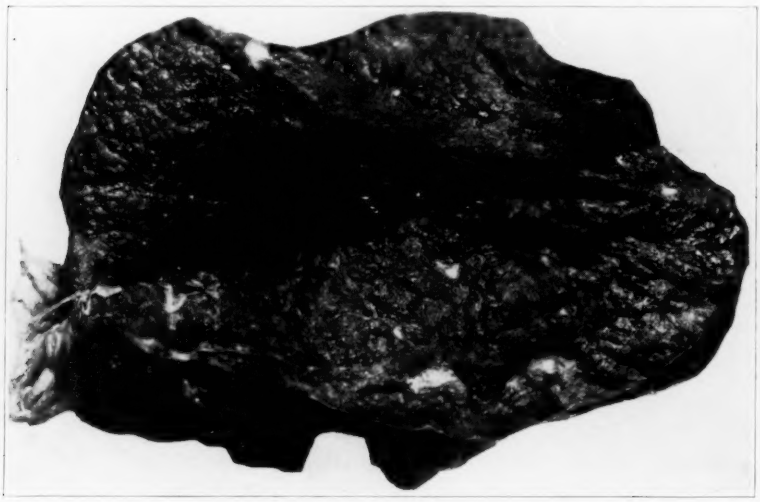

Fig. 11 (case 4).—Cut surface of the spleen, showing calcified hematogenous tuberculous foci.

primary focus may or may not be found, but I believe that it is important for physicians to train themselves to regard these cases not as instances of tuberculosis of the cervical nodes, tuberculous dactylitis or tuberculosis of the knee but as cases of systemic tuberculosis. Almost certainly even the child with clinical evidence of nothing but a tuberculous knee will show pathologic evidence of tuberculosis elsewhere. I believe the time is coming when it will be thought impossible to devote a hospital to one aspect of tuberculosis, such as disease of the bones and joints, to the exclusion of other forms. In this group, too, evidence of protracted dissemination may be observed. I now have under observation a child with tuberculous dactylitis of one month's duration. One year ago she had a primary focus, followed by hematogenous extension to the eyes

and cervical nodes. It may be that ultimately it will be found that many patients with tuberculosis running a long course and with extensive lesions are suffering from chronic hematogenous dissemination from one or more foci.

CASE 5.—The case of R. P., a Puerto-Rican, was an example of the third type. He was brought to the clinic when 1 year old because of dactylitis of the left index and middle fingers. Two months previous to his admission the cervical nodes had been markedly swollen, and they were still enlarged and discrete. The reaction to the tuberculin test was positive with 0.01 mg. There soon developed a lesion of the right cheek, which was not tender but indurated and dark red (fig. 12*A*); this was diagnosed as scrofuloderma by several dermatologists. A roentgenogram revealed a shadow in the upper lobe of the left lung. The dactylitis of the index finger showed progressive destruction (fig. 12*B*), and tubercle bacilli of the human type as differentiated by culture were easily demonstrated in the

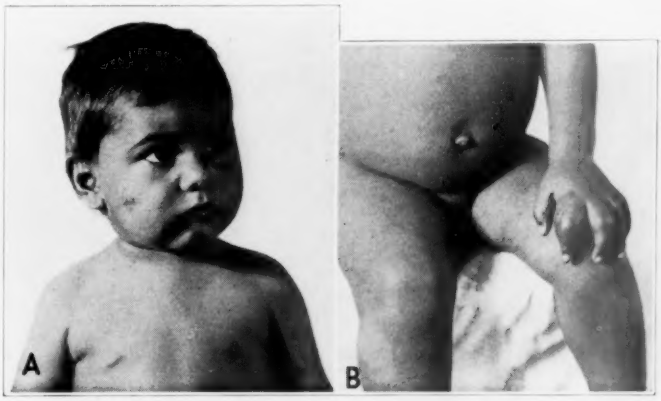

Fig. 12 (case 5).—Appearance of the patient at 23 months, showing scrofuloderma on the right cheek and dactylitis of the index and middle fingers.

purulent discharge. Six months later the roentgenogram of the lungs showed nothing abnormal. At 3 years of age the lesion of the face was clinically diagnosed as lupus vulgaris and showed the typical "apple jelly" nodules. The general condition was excellent. The lungs were normal on roentgen and physical examinations. All that remained of the dactylitis was a slight thickening of the index finger which was a little crooked and which showed excellent healing on roentgen examination.

In the fourth type of case which is recognized clinically, bacillemia may be occult. Probably this form should be regarded purely as a part of the primary tuberculous infection. In such a case the general condition of the child may seem normal; the nutritional state may be good, and fever may be, and often is, absent. Enlargement of the superficial nodes and of the spleen and evidences of metastases in the skin, such as papulonecrotic tuberculids, are the most common clinical evidences of dissemination, although all these signs may be absent.

A case which illustrates occult bacillemia occurred in the wards of Bellevue Hospital last year.

CASE 6.—C. G., a white boy 8 days of age, was admitted as a healthy infant. He had never been breast fed but had been with his mother, who had tuberculosis with bacilli in the sputum, for the first six days of his life. He weighed only 4 pounds and 12 ounces (2,154.6 Gm.), but his general condition and gain in weight were good. Two weeks after his admission a red throat and a low grade fever developed, which continued for three weeks. After this he gained more slowly but otherwise seemed well until extensive furunculosis developed when he was 9 weeks old. His temperature soon reached 101 F. daily, and he showed progressive loss of weight until his death at 12 weeks of age. Reactions to tuberculin tests were negative at the ages of 6 and 8 weeks, but he showed a positive reaction to 0.2 mg. of tuberculin at 10 weeks of age. The roentgenogram of the lungs, at first negative, showed an area of infiltration at the root of the left lung when he was 10 weeks of age.

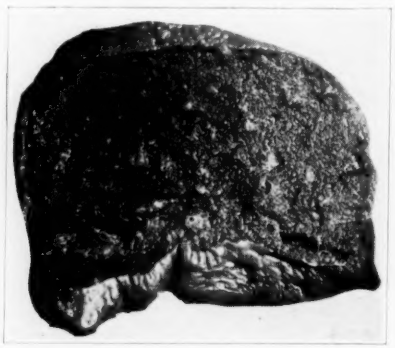

Fig. 13 (case 6).—Cut surface of the spleen, showing hematogenous foci of varying sizes.

The autopsy revealed a caseating primary focus in the apex of the lower lobe of the left lung with beginning formation of cavities; caseous involvement of the regional bronchopulmonary nodes on the left side; tubercles of unquestionable hematogenous origin and of miliary size in the apexes of both lungs, and tubercles of varying sizes in the spleen (fig. 13) and in the liver.

This case was one of hematogenous dissemination from a primary focus to the lungs, liver and spleen, which, because of the age of the child and the appearance of the tubercles, must assuredly have followed shortly after, if it was not coincident with, the appearance of the primary focus and which could not have been diagnosed clinically at that stage. This case is an example, too, of the occult type of repeated hematogenous dissemination, since the variation in the size of the metastases in the liver and spleen is evidence of repeated dosage. Many pathologists have noted scattered fresh or calcified tubercles in the spleen or elsewhere as accidental observations in persons who did not die of tuberculosis. Such cases fall into the group of those of occult bacillemia. Apical tubercles

may also be noted accidentally at autopsy, or they may become visible in the living patient by means of the roentgenogram. For a long time I have been interested in this form of hematogenous pulmonary tuberculosis, which when carefully sought has been observed as a postprimary development in an increasing number of cases. Huebschmann [10] was the first pathologist to draw attention to isolated foci in one or both apexes, which he regarded as a part of the picture of hematogenous extension. According to his description fresh tubercles may be like those seen in the lungs in case 6—small grayish-yellow nodules of miliary size just under the apical pleura—or there may be an inflammatory exudate or evidence of healing such as indurated scars of calcification, around the tubercles. Simon [11] in 1921 first drew attention to these lesions as revealed in roentgenograms. I first diagnosed a case by this means in 1924.

CASE 7.—S. S., a white child 18 months old, was sent to this hospital after an attack of measles because at a routine examination a positive tuberculin reaction had been discovered. The child was well nourished; there were no abnormal findings on physical examination, and fever and symptoms were absent. The roentgenogram, however, revealed an infiltration surrounding the hilus of the right lung. This resolved slowly, but eighteen months later calcifications appeared at both apexes (fig. 14). The picture has remained unchanged for about ten years.

These apical foci may vary from lesions of miliary size to large, irregular masses. Clinically, they behave like foci due to reinfection; the exudative reaction about them, when present, is likely to be less marked and of shorter duration than the infiltration around a primary focus, and they apparently calcify more quickly than does the primary focus. In fact, they usually show deposits of calcium when first seen in the roentgenogram.

CASE 8.—The roentgenogram of C. A., a white child 10 years old, showed calcified primary foci in the lower lobe of the right lung and clear apexes. Six months later an indefinite shadow at the apex of the right lung appeared, which was unrecognized at the time, and in another six months calcification of the apical lesion was noted. No abnormal physical signs were heard over the lungs at any time.

I agree with Simon [11] that these lesions are probably hematogenous in origin. Occasionally a large lesion is difficult to distinguish from a primary focus unless serial pictures, extending over a long period, are available, but the lesion is not accompanied by enlargement of the regional nodes and it usually calcifies more quickly than the primary

10. Huebschmann, P.: Pathologische Anatomie der Tuberkulose, Berlin, Julius Springer, 1928.

11. Simon, G.: Sekundaere Streuherde der Lunge, insbesondere die frühen Spitzenherde, in Engel, S., and Pirquet, C.: Handbuch der Kindertuberkulose, Leipzig, Georg Thieme, 1930, vol. 1, p. 470.

infection. Moreover, as occurred in case 8, a calcified primary focus is often present elsewhere before the appearance of these lesions. Bronchogenic aspiration is an unlikely explanation of the origin of these foci because of their position. For the same reason it does not seem reasonable to suppose that these apical foci are due to exogenous reinfection, especially since it is known that first infections, which are conceded to be of exogenous origin, usually occur in the lower part of the upper lobe or in the middle or lower lobes.

The relation of the "Simon foci" to apical tuberculosis of later development or to the so-called tuberculosis of adults can only be conjectured. They are often first discovered in adult life, and their

Fig. 14 (case 7).—Calcified deposits in the supraclavicular fields of both lungs following primary tuberculous infection.

significance as evidence of previous hematogenous extension is not always recognized. No one, to my knowledge, has ever seen these lesions progress clinically into chronic phthisis. I am at present observing with great interest a group of patients with lesions of this type. It is certain that obvious hematogenous dissemination in the lungs, such as those which occurred in the marked protracted cases in this series, may break down and exactly simulate the clinical picture of chronic ulcerative tuberculosis. If these small foci of hematogenous origin prove to be a frequent source of the subapical infiltration of chronic organic phthisis, another link in the chain of knowledge concerning the pathogenesis of pulmonary tuberculosis will be furnished. Exogenous reinfection as a

cause of apical tuberculosis cannot be discarded. A recent heavy exposure to tuberculosis is often mentioned in the history of adolescent boys and girls and young adults with subapical infiltrations. But it may be that exogenous reinfection causes an activation of older hematogenous lesions, which subsequently break down and lead to bronchogenic extension.

SUMMARY

The theory is presented that hematogenous dissemination of tuberculosis follows the establishment of the primary complex in the majority of cases. Clinical, bacteriologic and pathologic proof exists that this may occur. Four groups of cases ranging from instances of the marked forms of protracted disseminated hematogenous tuberculosis to those of occult bacillemia are described, and typical clinical cases are presented. The possible relationship of early hematogenous apical dissemination ("Simon foci") to later apical tuberculosis is discussed.

COMPARATIVE VALUES OF CUTANEOUS, PERCUTANEOUS AND INTRACUTANEOUS TUBERCULIN TESTS IN CHILDREN

SPECIAL REFERENCE TO SENSITIVENESS OF THE PLASTER TEST

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The diagnostic importance of the tuberculin test is generally recognized, although the specificity of the reaction is still being discussed in the literature. There is, however, much less agreement as to the choice of the most practical method.

In 1890 Koch introduced the generalized or subcutaneous tuberculin test. In 1902 Branner observed a local reaction of the skin around the site of injection of the therapeutic dose of tuberculin then in use.

It was not until Pirquet discovered the exceeding sensitivity of the skin as an indicator of tuberculosis that one was able to study tuberculosis in its character of an endemic disease. A few months after Pirquet had made known his cutaneous method, efforts were made to modify it, both in the direction of increasing its sensitivity and in that of avoiding traumatism. The efforts in the first direction led to the development of the Mantoux-Mendel intracutaneous test (described by Mantoux in 1908) and of the Hamburger-Monti puncture test (1909), and in the second direction, to the evolvement of Moro's percutaneous test, and various modifications of Pirquet's test (those of Lautier, Lignière, Kashara, Blumenau, Schmidt and Wegerer, Feer, Grass and Brandes). Various further tests of the reactions of the mucous membranes were evolved, such as the ophthalmoreaction (Calmette, Wolff and Eisner), the rhinoreaction (Lafite and Dupant and Molinier and Möller), the urethral reaction (Oppenheim and Pagano), the vaginal reaction (Schwab and Schnürer) and the anal reaction (Calmette, Breton, Ruteman and Lissauer).

These reactions of the mucous membranes are now only of historical interest so far as human pathologic processes are concerned.

In accordance with the writings of Habetin,[1] tuberculin tests may be divided into three groups:

1. Those using the method of trauma in the narrower sense (Pirquet, Feer, Brandes and Grass).

From the Medical Department of the Samaritan Hospital for Children's Diseases, Stockholm; Dr. Nils Malmberg, Chief.

1. Habetin, P.: Die Tuberkulinsalbenpflasterprobe, Wien. klin. Wchnschr. **41**:703, 1928.

2. Those using the method of friction, or trauma in a wider sense (Moro, Ligniére and Wegerer).

3. Those using the method of contact (Lautier, Blumenau, Kashara, Habetin, Wolff and Malmberg-Fromm).

Most of these tests are founded on the same principle, namely, that of bringing the tuberculin into touch with the more deeply situated epithelial cells.

In pediatric practice, in which one wishes, so far as possible, to eliminate every form of traumatism, the contact method has been the one most employed. Moreover, the skin of the child is delicate and thin, and it therefore reacts more readily than that of the adult. In 1907 Moro and Doganoff [2] described the method of inunction, subsequently elaborated by Moro.[3] In the following year Moro made an attempt to prepare a plaster from the ointment which he had made but was unable to overcome the technical difficulties. In 1913 the percutaneous method was improved by Wegerer,[4] and it was further modified in 1919 by Hamburger and Stradner. Widowitz [5] in 1922 found that the number of positive reactions to the test increased if before inunction the skin was cleansed with ether until it became hyperemic. In a subsequent investigation K. Hille [6] found that this increase was about 30 per cent. It was not until 1931 that Malmberg and Fromm [7] succeeded in obtaining a technically satisfactory plaster, so made that it contained 1 drop of tuberculin per square centimeter.

The technic for application of the plaster test is simple. After the skin (usually that over the manubrium sterni) is cleansed with ether, a plaster is applied as a control, and about 1 cm. below this the tuberculin plaster is applied (fig. 1 *A*). For infants and nervous children it seems expedient to apply an ordinary adhesive plaster over the other two to prevent them from being pulled away (fig. 1 *B*). The reaction is read after forty-eight hours. In the positive reaction the skin beneath the tuberculin plaster is found to present, either sparingly or more closely according to the intensity of the reaction, highly red

2. Moro, E., and Doganoff, A.: Zur Pathogenese gewisser Integumentveränderungen bei Skrofulose, Wien. klin. Wchnschr. **20**:933, 1907.

3. Moro, E.: Ueber eine diagnostische verwertbäre Reaktion der Haut auf Einreibung mit Tuberkulinsalbe, München. med. Wchnschr. **55**:216, 1908.

4. Wegerer, F.: Studien über Tuberkulin-Percutanreaktionen, Med. Klin. **9**:575, 1913.

5. Widowitz, P.: Ueber eine modifizierte perkutane Tuberkulinprobe, München. med. Wchnschr. **69**:233, 1922.

6. Hille, K.: Zur Tecknik der perkutanen Tuberkulinreaktion nach Moro, Arch. f. Kinderh. **88**:14, 1929.

7. Malmberg, M., and Fromm, B.: Die Tuberkulinpflasterprobe: Eine vereinfachte Methode zur Ausführung der perkutanen Tuberkulinprobe, Acta pædiat. **10**:433, 1931.

papules the size of a pinhead (fig. 2). In the negative reaction the skin remains unaltered. Occasionally a reaction may also be obtained under the plaster used as a control. The exceedingly few cases in which

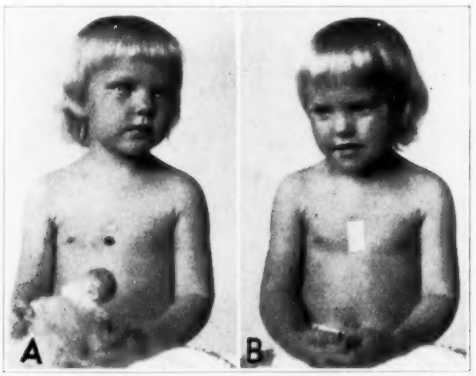

Fig. 1.—Photograph showing the technic of the plaster test. *A* shows the sites of application of the plaster used as a control and of the tuberculin plaster; *B*, the protective adhesive plaster.

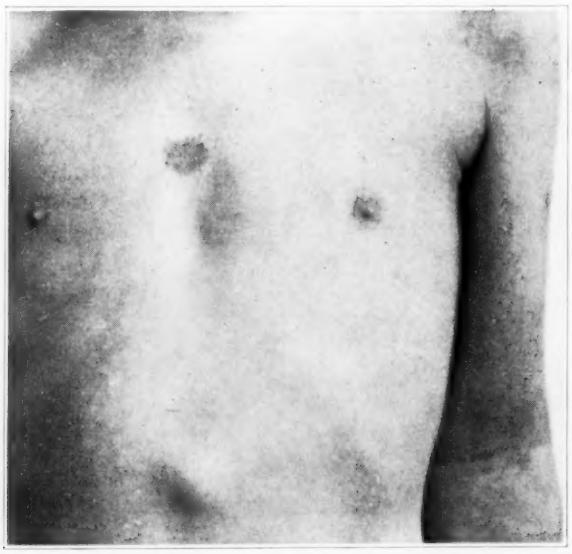

Fig. 2.—A positive reaction elicited by the tuberculin plaster test.

this has happened have occurred in tuberculous patients with exudative diathesis.

Numerous authors have made investigations of the comparative values of the various tuberculin tests in order to determine their reliability. With regard to the diagnostic effectiveness of Pirquet's test,

which seems to be the one most frequently employed, the opinions expressed in the literature differ considerably. D'Arcy Hart [8] in 1932 analyzed the results obtained by 42 authors in the study of a total number of 4,787 cases of clinically manifest tuberculosis. No reaction to the Pirquet test was obtained in 16 per cent of these cases. If only the cases occurring in children are included, the number is raised to 23 per cent. Wallgren [9] expressed the opinion that about 20 per cent of the cases of manifest tuberculosis are missed by Pirquet's test. Tisdall and Brown [10] found the corresponding value to be as high as 41.9 per cent, and Greengard and Nichamin,[11] 34.6 per cent. They therefore considered Pirquet's test greatly inferior not only to tests by the intracutaneous but to those by the percutaneous method.

With the percutaneous method Stradner obtained positive results in 84 per cent of the cases; Wallgren, in 83 per cent; Czickeli,[12] in 80.3 per cent; Greengard and Nichamin, in 82.1 per cent, and Harms and Seitz in 94.8 per cent. Drucker [13] and Holm, Danish authors, maintained, however, that the percutaneous method is less sensitive in patients of more advanced years. The latter author expressed the view that not less than 50 per cent of the cases occurring in persons past 14 years of age are missed with the percutaneous method.

With regard to the intracutaneous or, as it is usually called, Mantoux's test, the majority of authors seem to agree that this test is superior both to those by the cutaneous and to those by the percutaneous method. Duken [14] considered it even too sensitive and stated (1927) as his opinion: "A positive intracutaneous reaction is to be absolutely accepted as positive only if subsequent tests also result positively." Bäumler [15] supported this view, and similar statements were made by Moro, Nobel and Rosen.

With a view to determining the reliability of the tuberculin plaster test, there have been carried out at the medical department of the

8. Hart, P. D'Arcy: The Value of Tuberculin Tests in Man, Medical Research Council, Spec. Rep. Ser. 164, London, His Majesty's Stationery Office, 1932.

9. Wallgren, A.: Hamburgers perkutane Tuberculinreaktion, München. med. Wchnschr. **71**:1017, 1924.

10. Tisdall, F. F., and Brown, A.: Relative Values of Different Tuberculin Skin Tests, Canad. M. A. J. **16**:939, 1926.

11. Greengard, J., and Nichamin, S.: The Diagnostic Tuberculin Reaction, J. Pediat. **4**:393, 1934.

12. Czickeli, H.: Ueber die Brauchbarkeit verschiedene Tuberkulinisierungsmethoden zu diagnostischen Zwecken, Monatschr. f. Kindh. **29**:242, 1925.

13. Drucker, P.: Dansk ped. selskabsförh. 1931-1933, p. 99.

14. Duken, J.: Unstimmigkeiten in der praktischen Verwertung der Tuberculindiagnostik, Ztschr. f. Kinderh. **43**:331, 1927.

15. Bäumler, O.: Zur Prognose der Tuberkulose der ersten beiden Lebensjahre, Arch. f. Kinderh. **84**:136, 1928.

Samaritan Hospital, during 1933 and until July 1 of the present year, investigations of the comparative values of this test and of the Pirquet and the Mantoux test. The aggregate number of patients was 2,183, and the ages ranged from 3 days to 15 years. A negative reaction was elicited, both to the plaster and to the Pirquet test, in 1,838 of these patients, and a positive reaction to both tests in 307 patients. Thus the reactions to the tests were in agreement in 98 per cent of the cases. By way of comparison it may be stated that Gunther, at the Crown-Princess Louisa's Hospital in Stockholm, obtained agreement in the reactions to the two tests in 94 per cent of 402 cases, and Monrad [16] found correspondence in the results obtained with the Moro and Pirquet tests in 97 per cent of 13,000 cases.

In 10 cases Pirquet's test gave a negative reaction, but the reaction to the plaster test was positive; in all these cases there was a positive reaction to Mantoux's test, as shown in the following tabulation:

	Patient		
Dose, Mg.	Number	Sex	Age, Years
0.1	1	M	3
0.1	1	M	9
0.1	1	M	10
0.1	1	M	13
0.1	3	M	8
1.0	1	F	10
1.0	1	F	8
1.0	1	F	11

All these patients were afebrile; i. e., the temperature did not exceed 37.5 C. (99.5 F.) at the time the tests were given.

In 28 cases there was a febrile condition. The reactions given by these patients were as follows:

1. Patient 1 showed a positive reaction to the Pirquet test but a negative reaction to the plaster test. This patient proved to have tuberculous meningitis and died three days after admission to the hospital.

2. Patient 2 showed an uncertain reaction to the Pirquet test and a negative reaction to the plaster test. A negative reaction was obtained to Mantoux's test with as high a dose as 5 mg.

3. Patient 3 showed a positive reaction to the Pirquet test, but a negative reaction to the plaster test on admission; when a fortnight later the fever had subsided, a renewed plaster test gave a positive reaction. The patient had pleuritic effusion.

4. Patients 4 to 11 showed a negative reaction to both tests. A positive reaction to the Mantoux test with 0.1 mg. was later elicited in 3 of the patients and a positive reaction with 1 mg. in 5 patients.

16. Monrad: Dansk ped. selskabsförh., 1931-1933, p. 97.

One of the patients who showed a positive reaction with 0.1 mg. had a normal roentgenogram.

5. Patients 12 to 28 showed a positive reaction to the plaster test but a negative reaction to the Pirquet test. In 11 of these patients a positive reaction was elicited to the Mantoux test with 0.1 mg., and in 6 patients with 1 mg.

That no definite conclusion can be drawn as to the sensitivity of the cutaneous and percutaneous tests in febrile states has long been known, yet the tuberculin plaster test seems to be greatly superior to the Pirquet test in febrile states also.

Of the 1,838 patients in whom a negative reaction was elicited both to the plaster and to the Pirquet test, 806 were further tested by Mantoux's method. Of this number 11 (1.25 per cent) reacted positively as follows:

Dose, Mg.	Patient Number	Sex	Age, Years
0.1	1	F	12
0.1			
5	1	F	2
5	1	M	9
1	1	F	8
1	1	M	4
1	1	M	5
1	1	M	8
1	1	M	9
1	1	M	12
1	1	M	10

Two of the patients, a boy of 10 years who reacted to 1 mg. and a girl of 2 years who reacted to 5 mg., had normal roentgenograms.

Of the 307 patients with positive reactions, 13 had a stronger reaction to the Pirquet test and 31 to the plaster test. In only 2 of these cases did the control test also give a reaction and, as already mentioned, these were cases of tuberculosis associated with exudative diathesis.

With regard to the sustaining qualities of the plaster, it may be mentioned that in tests of twelve plasters, which had been made up for two years, with patients having manifest tuberculosis as subjects, a powerful positive reaction was given in all cases.

CONCLUSIONS

In the present investigation the plaster and the Pirquet test yielded consistent results in 98 per cent of the cases. In 0.5 per cent of the cases the plaster test gave a positive reaction while the reaction to the

Pirquet test was entirely negative. In febrile states the plaster test proved much more sensitive than the Pirquet test. Even when both tests gave positive results the plaster test, in the majority of cases, yielded the more powerful reaction. Were the plaster test alone employed, only 1.25 per cent of the positive reactions would fail to be detected.

LATE INFANTILE AMAUROTIC IDIOCY WITH MARKED CEREBRAL ATROPHY

CLINICAL AND ANATOMIC REPORT OF A CASE

RICHARD RICHTER, M.D.
AND
ARTHUR H. PARMELEE, M.D.
CHICAGO

As recently as 1909, Schaffer [1] made the statement, which he has since greatly modified, that infantile amaurotic family idiocy was characterized by no macroscopic anatomic changes. Since that time a number of brains of persons with this disease showing gross changes of greater or lesser magnitude have been reported on, but these are not so numerous that observations on an additional one are without interest. Moreover, any unusual data in the realm of amaurotic idiocy are of value, since this condition occupies so important a position as the paradigm of heredodegeneration of the nervous system and as a definite anatomic species within the great group of the idiocies. This, we think, justifies adding the present report to a literature already abundant and not a little repetitious.

REPORT OF CASE

History.—The patient, a boy 5 years old not of Jewish parentage, was admitted to the service of one of us (A. H. P.) at the Presbyterian Hospital, on Sept. 11, 1928. The birth of the child was normal, following a normal pregnancy, which was the mother's second. The weight at birth was 9 pounds (4,082.33 Gm.). The infant was breast fed for eight months, and the subsequent dietary history was uneventful. The child held his head up at 5 months, sat up at 8 months and walked at 1 year. He was able to say "mama" at 1 year.

Nothing unusual was observed by the parents until the child was 14 months old, when without any apparent preceding illness he became fussy, lost his appetite and ceased to gain properly. During the next two weeks he stopped walking and sitting up, and from this time he did not talk. During the ensuing year both arms and legs became paralyzed, and they remained so. In the same period it became difficult to feed him because he gagged when food was put into his mouth and seemed not to be able to swallow. It was the mother's opinion that the child could see and hear. There was no history of convulsions. The child had had measles and chickenpox at 2 or 3 years.

The father was 51 years old and the mother 32; both were well. The father had two healthy children by a previous marriage and there was one sister of the

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Read at a meeting of the Chicago Neurological Society, Jan. 18, 1934.

From the Departments of Neurology and Pediatrics of Rush Medical College.

1. Schaffer, K.: Ueber das morphologische Wesen und die Histopathologie der hereditär-systematischen Nervenkrankheiten, Berlin, Julius Springer, 1926.

patient, a girl of 6, who was well. Except for a maternal uncle who was not normal and lived only one year there was no suggestive family history.

Physical Examination.—Examination revealed a very much emaciated child, weighing 21 pounds (9,525.43 Gm.), with poor tissue turgor, a thin pointed face and a scaphoid abdomen. The circumference of the head was 18¾ inches (47.63 cm.). The chest and abdomen were normal. The child lay with the arms tightly flexed and adducted and with the hands clenched. There were flexor contractures of the arms. The legs were in a position of slight flexion and adduction; the toes were in a position of sharp plantar flexion. There was no evidence of any degree of awareness of the environment. Twitching of the hands and arms occurred constantly. From time to time the child uttered a weird "hydrocephalic" cry. All the deep reflexes were greatly exaggerated, but there was no Babinski sign and no clonus. The pupils were wide and equal and reacted very sluggishly to light. Inconstant jerky nystagmoid movements were occasionally observed.

Neurologic Examination.—Dr. Peter Bassoe, who was the neurologic consultant in the case, made the following observations:

Sept. 21, 1928: The position of the extremities suggested decerebrate rigidity with hyperflexion of the elbows, wrists and metacarpophalangeal joints and less marked contraction of the knees, ankles and metatarsophalangeal joints. When the thighs were flexed and the knees were extended there was partial extension of both elbows, which occurred also when the thighs were forcibly abducted. Rotation of the head did not produce any movement of the extremities. Stroking the soles of the feet increased the flexion at the hip, knee and toes. Passive extension of one knee caused prompt adduction of the opposite hip. Tapping of one knee caused a contraction of almost all the muscles of both lower extremities. The ankle reflexes were much increased. There was no clonus. There were often rhythmic jerkings of the muscles of the eyes and of the hands. Hearing was probably preserved, at least to some extent, as the child winked his eyes when a noise was made.

September 25: The child was lying quietly with the eyes open, making chewing movements. The elbows, wrists and fingers were hyperflexed, with the thumbs held between the first two fingers. The legs were straight, and the toes and feet were in a position of plantar flexion. Prolonged ankle clonus was obtained on both sides. Stroking the soles of the feet caused marked combined flexion of the hip and knee and flexion of the big toes, and on the right side it started an ankle clonus. An abdominal reflex was obtained in all four quadrants.

March 14, 1929: When the head was rotated far to the left there were clonic spasms of the plantar flexors of the right foot, lasting a few seconds, and the left leg was abducted. Rotation of the head to the right caused the patient to cry and to make slight to-and-fro movements of the left knee. Flexion of the neck caused no movement of the extremities. The responses on rotation were not constant or uniform.

Ophthalmologic Examination.—An examination by Dr. Thomas D. Allen revealed that the child was blind. Both disks were gray-white, and no blood vessels were seen in either retina. A slight peppery appearance of both retinas was noted. There was no cherry-red spot at the maculae.

Laboratory Observations.—The urine was normal. A blood test showed: hemoglobin, 78 per cent; red cells, 5,300,000; white cells, 15,800, with a relative increase of mononuclear cells, and a negative Wassermann reaction. Examination of the spinal fluid by Lange's method revealed: colloidal gold curve, 1122100000; total

protein, 41.6 mg. per hundred cubic centimeters; sugar, 87.7 mg.; chlorides, 737 mg.; urea, 10.3 mg.; creatinine, 1.2 mg.; nonprotein nitrogen, 15.5 mg., and cholesterol, none. Anteroposterior and lateral roentgenograms of the skull showed no abnormalities.

Course.—The patient remained in approximately the same state as on admission, with some increase in rigidity, until his death on June 22, 1929, nine months after admission. During this time the child was fed entirely by gavage. From the time of admission he had had an intermittent fever with a temperature up to 101 F. Terminally this reached 104 F. From time to time albumin, casts and a great deal of blood appeared in the urine. Death followed bronchopneumonia, presumably the result of aspiration of vomitus.

The diagnosis lay between Schilder's disease and an atypical form of Tay-Sachs' disease.

Macroscopic Observations at Autopsy.—In addition to the changes in the nervous system the principal findings at necropsy, done by Dr. C. W. Apfelbach,

Fig. 1.—The right cerebral hemisphere, showing universal convolutional atrophy.

were: extensive bronchial aspiration of gastric contents; acute emphysema of the lungs; extensive bilateral lobular pneumonia; bilateral fibrinous pleuritis, and marked emaciation. Other than this there were no gross or microscopic abnormalities of the organs of the trunk, particularly with reference to the spleen and liver.

Gross Appearance of the Nervous System.—The brain, hardened in a solution of formaldehyde, weighed 416 Gm. The leptomeninges covering the hemispheres of the brain were everywhere somewhat more opaque than normal and had a glassy, gelatinous appearance, as if from edema. This was greatest over the frontal lobes. The meninges of the base and those covering the cerebellum and brain stem appeared to be normal. The foramina of Luschka were wide and patent; the foramen of Magendie had been destroyed by removal of the brain. The cisterna magna was enormously enlarged, and the cerebellum presented a marked concavity on its lower surface, corresponding to the enlarged cisterna. The cisterna around the chiasm was much enlarged, forming a cavity 20 mm. wide, 30 mm. long and 17 mm. deep, into which the tuber cinereum protruded. The principal

markings of the cerebral hemispheres were present and showed no marked abnormality, but the identification of them was made difficult by the exaggerated prominence of small sulci occasioned by the extreme general atrophy of the cortex which was equal in all parts of the hemispheres (figs. 1 and 2). The atrophy was of such degree that the sulci stood open and their depth could easily be seen without spreading them apart. Both cerebral hemispheres felt vesicular on palpation and could easily be indented, as though the cortex were the shell of a hollow structure.

Similarly, there was extensive atrophy of the brain stem and cerebellum. The cerebral peduncles were shrunken so that the interpeduncular fossa was a pit 12 mm. wide, 9 mm. long and 6 mm. deep. The pons was decreased more than half and was wrinkled, presenting longitudinal depressions. There was marked enlargement of the fourth ventricle; the distance from the posterior end of the iter to the calamus scriptorius was 3 cm. and the ventricle measured 2 cm. at its widest part; the greatest depth was 14 mm. There were no anomalies of the external

Fig. 2.—The left cerebral hemisphere.

configuration of the brain stem, including the floor of the fourth ventricle. The cerebellum weighed 58 Gm. The average width of the folia was 1.4 mm. The cerebellar peduncles were correspondingly decreased. The cerebellar atrophy was proportionate in all its parts and to that of the rest of the brain (fig. 3).

Both optic nerves were very small, measuring 2 mm. in diameter, and the chiasm and optic tracts were correspondingly reduced. The olfactory tracts were reduced to a breadth of 2 mm. The remaining cranial nerves were normal though perhaps small in caliber.

The arteries of the base had the usual arrangement, and their linings were smooth and glistening.

Surfaces made by cutting the brain just anterior to the chiasm revealed a pronounced dilatation of the ventricular system, which was symmetrical. The lateral ventricles measured 4.5 by 3.5 cm. in their greatest diameter. The foramina of Monro measured 12 by 8 mm. The ventricular surfaces were not nodular; the lining was smooth. The fifth ventricle was well developed. The encasing brain tissue above in the region of the superior and middle frontal convolutions and below in the region of the lower part of the insula was about 1 cm.

thick; in the upper part of the insula it was in places from 2 to 3 cm. thick. The corpus callosum at this level was represented by a thin membrane, 13 mm. wide and less than 1 mm. thick. Since the demarcation between the gray and the white matter was very indistinct, it was difficult to measure the thickness of the cortex, but it was greatly reduced.

At a level 12 mm. posterior to the infundibulum the expansion of the ventricles was striking. Here the lateral ventricles were 3 by 3 cm. in greatest diameter, with the left inferior portion measuring 2.5 by 4 cm. and the right, 2 by 3 cm. The third ventricle at this level was 2 cm. in the greatest vertical and transverse diameters. Posterior to the level of the posterior commissure the inferior and posterior horns and the body of the lateral ventricles were continuous and merged into one enormous cavity. The opening of the aqueduct of Sylvius was easily seen at the posterior end of the third ventricle and was 5 mm. in diameter. The length of the third ventricle from the lamina terminalis to the posterior commis-

Fig. 3.—The posterior aspect of the brain, showing cerebellar atrophy.

sure was 24 mm. In the posterior part of each lateral ventricle was a strand of tissue about the caliber of a coarse linen thread, passing from the lateral to the medial wall. The distance from the top part of the lateral ventricle to the surface of the overlying convolution was 1 cm., and from the outer border of the internal capsule to the surface of the insula, 2.5 cm. In this place (at the level of the massa intermedia) the region of the thalamus, corpus striatum, internal capsule and centrum ovale was a bridge of tissue from 2 to 2.5 cm. across and 1.5 cm. high with a thickness medially from the massa intermedia to the posterior commissure of 12 mm. The boundaries between the basal nuclei were extremely indistinct. The region of the corpus striatum was particularly reduced in size. The internal capsule, represented by a few coarse fiber bundles, was 3 mm. wide on both sides (fig. 4).

The brain tissue everywhere was very firm when cut, especially that of the cerebellum.

The meninges of the spinal cord, both the dura and the pia-arachnoid, were entirely normal. There was no appreciable reduction in the number or size of the spinal roots. The length of the cord from the filum terminale to the first cervical segment was 24 cm. as compared with a length of 48 cm. for a normal cord from a child of the same age. The circumference of the cord was somewhat decreased at all levels, the diameter being about 1 mm. under the normal measurement. The cut surfaces of the cord were normal except that there appeared to be a relative reduction of white matter at the dorsal and lumbar levels.

Microscopic Appearance of the Nervous System.—Ganglion Cells: In sections prepared by the Nissl method there was a marked reduction in the number of ganglion cells of almost every portion of the central nervous system, and of those remaining there was not one which did not show advanced degenerative changes. The details of these changes varied between the different nuclear groups and, to some extent, between individual cells of the same group in accordance with the

Fig. 4.—A frontal section, 12 mm. posterior to the infundibulum, showing atrophy of the brain stem and of the basal ganglions and marked disappearance of the white matter of the cerebral hemispheres with hydrocephalus.

degree of change present, but in general the alterations were uniform as well as universal. All the cells were swollen—some much more than others—so that their contours were convex. The larger cells tended to assume bizarre, elongated, fusiform or pearlike shapes; the smaller cells were more rounded. For the most part the cell processes were sparse and poorly stained. There was a variable reduction of Nissl substance, which usually was great and often complete. What Nissl substance remained stained fairly well and lay in the portion of the cell occupied by the nucleus. The remainder of the cell body stained from light gray-blue to gray-yellow and was homogeneous, although in some of the less badly damaged cells a delicate reticulum was discernible in this part of the soma, while in others fine dustlike granular particles were seen. The basal region of the cell body appeared to be particularly swollen with this homogeneous substance, and the nuclei were regularly displaced toward the opposite pole of the cell. In addition, there were a

variety of nuclear changes, among which vesicular swelling was the most common. Some of the nuclei contained numbers of small, very dark granules clustered along the nuclear membrane and on the nucleolus, and at times these were found scattered in the protoplasm of the cell, indicating complete nuclear disruption. In such cells the nuclear membrane was no longer visible. A common observation, especially among the smaller cells, was an extensive folding of the nuclear membrane, as if the nuclei had swollen and then burst and collapsed. These nuclei were frequently misshapen, lentiform or triangular. The nucleoli were well preserved except in those cells showing the most advanced state of degeneration. These

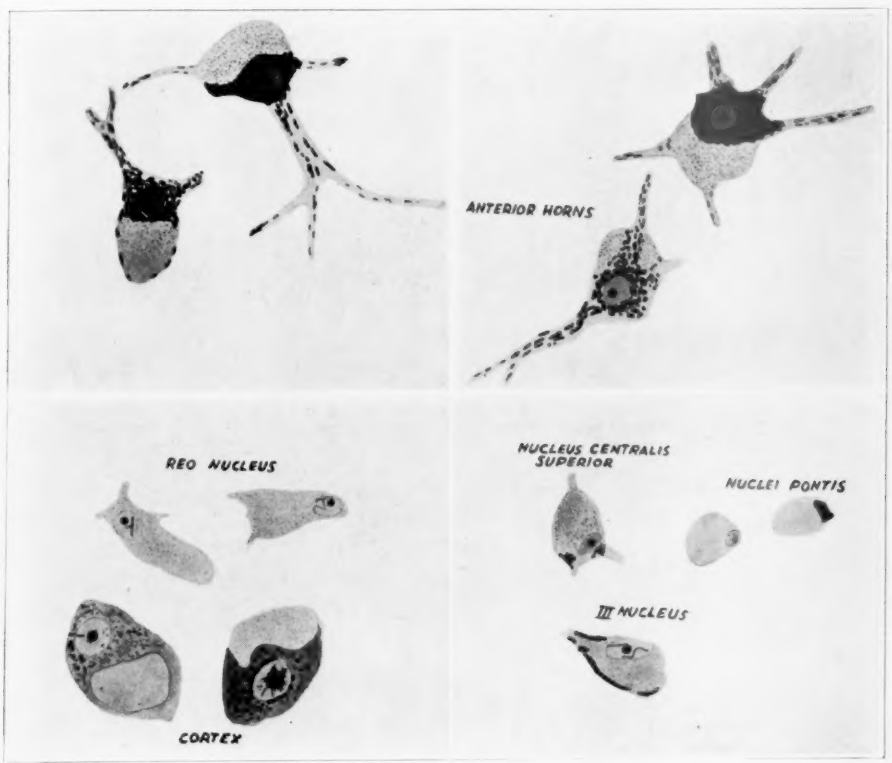

Fig. 5.—A reproduction of drawings of representative ganglion cells from various parts of the neuraxis delineated with Nissl's stain.

appeared as rounded, homogeneous, pale blue bodies without nucleus or nucleolus—veritable "cell shadows" (fig. 5).

The cellular architecture of the cortex no longer existed because of the disappearance of all the ganglion cells except a few isolated and greatly degenerated members of the fifth layer. This was true in all the regions of the hemispheres. The various nuclear groups in the region of the basal ganglions could no longer be identified with certainty because of the great contraction and distortion in this part of the brain from atrophy; but all the cells remaining in the striatum, pallidum and thalamus exhibited the type of change described, and likewise all the cells at every level of the brain stem. Here the large cells of the third nucleus and the

nucleus masticatorius were least affected. At all levels of the spinal cord there were the same changes in the cells of the anterior and posterior horns, although on the whole these cells were the least damaged of any and there was little or no reduction in their number. The dendrites of the anterior horn cells stained well and contained normal Nissl granules. They were uniformly enlarged, especially at the points of branching, but they presented no localized balloon-like expansion, nor was such expansion found elsewhere.

The folia of the cerebellar hemispheres and of the vermis were all markedly reduced, and the spaces between them were widened. The nerve cells of the

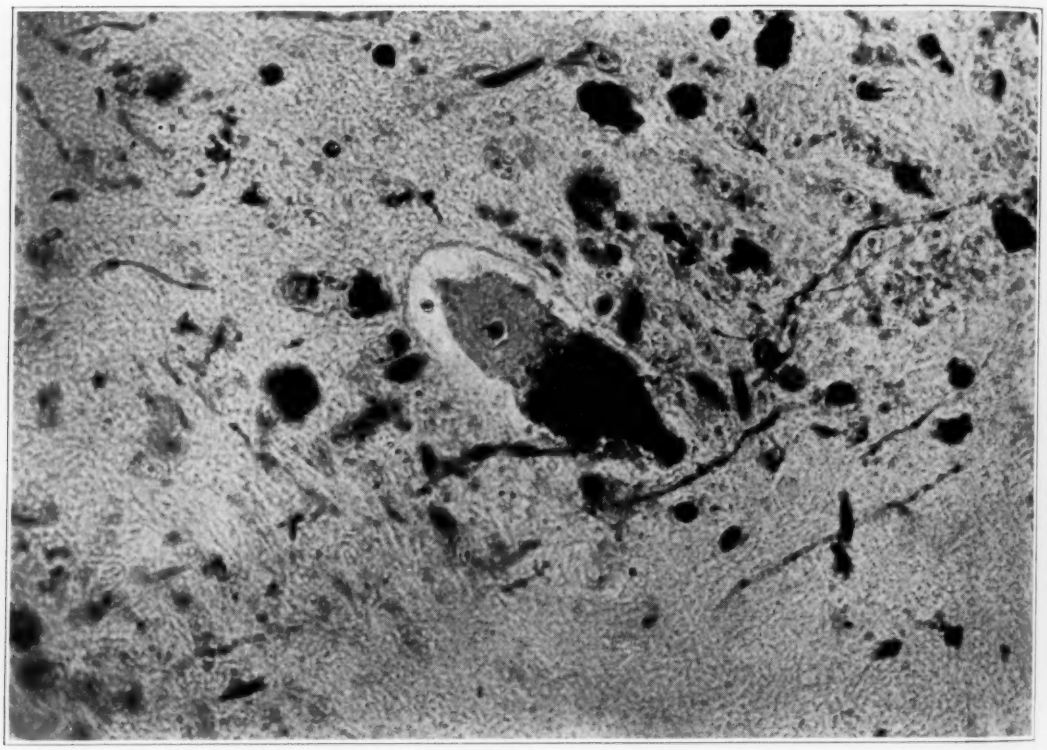

Fig. 6.—Prelipoid inclusions in a Purkinje cell and in glia cells. Stained with hematoxylin by Schaffer's method.

granular layer had disappeared completely and only an occasional, much dilapidated Purkinje cell was seen. The cells of the dentate nucleus had suffered the same changes as those of other nuclear complexes.

The lipoid deposits in the ganglion cells took only a faint yellow-pink tint with scarlet red and did not give a reaction for fat either with nile blue or with osmic acid. But with the Schaffer modification of the Weigert-Kulschitsky stain the cell bodies were seen to be more or less packed with rather small gray to black granules which were the lecithinoid granules of Schaffer (fig. 6). Many of the cells were so choked with this material that they appeared as opaque black masses without any discernible granular structure. The dendrites of some of the Purkinje

cells contained this material, and along a few of them was the characteristic balloon-shaped swelling of the infantile form of amaurotic family idiocy, heavily laden with the same granules.

In sections prepared with Bielschowsky's stain the same tumefaction of the cells was evident, with corresponding alteration in shape. Only a few of the cells preserved any indication of an intracellular fibrillar network. Instead they were occupied by an argentophilic detritus in the form of granules and threads which in some cases was concentrated in the center or at the basal pole of the cell and in others was scattered uniformly through it (fig. 7). When the intracellular reticulum was preserved at all, it was heavy, massive and strongly argentophilic and appeared to

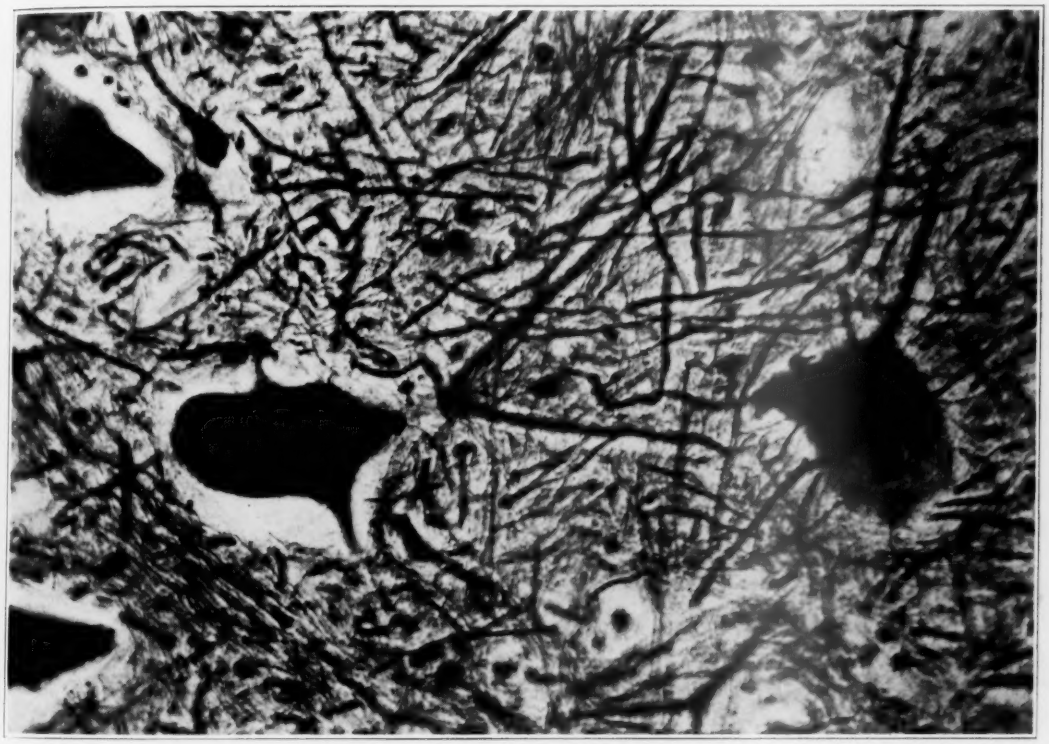

Fig. 7.—Anterior horn cells, showing the disappearance of intracellular fibrillary network and deposits of argentophilic substances. Bielschowsky stain.

enclose vacuoles of various sizes, some of which were quite large. On the whole, the dendrites were sparse, but when present they often possessed fairly well preserved neurofibrils. Neurofibrils were also seen skirting the periphery of some of the cell bodies. No balloon-shaped swelling of the dendrites was observed except in one or two of the Purkinje cells.

Myelin Sheaths: Sections of the cerebral cortex prepared by Spielmeyer's myelin sheath method were seen everywhere to be completely denuded of myelin fibers. In what remained of the white matter of the cerebral hemispheres only a few scanty fibers were seen, which were badly degenerated. In specimens stained by the Pal-Weigert method the region of the basal nuclei was

reduced greatly, as were all the structures in it. Moreover, there was a diffuse deficiency in myelin staining. The individual fibers were faintly stained and exhibited numerous swellings, but were not much fragmented. The internal capsule had practically disappeared, distorting all the relations of the structures. The globus pallidus was ill defined, owing to the great reduction of myelin in the structures which bounded it, especially in the internal capsule and the ansa lenticularis. Cross-sections of the brain stem at all levels showed a great reduction in area, the reduction being proportionate in the several structures. While there was some diffuse paleness of myelin staining throughout, the general topography was well preserved. The pyramidal tracts were very small and pale at all levels, though not completely degenerated, and the same was true for the mesial fillet. The cerebropontocerebellar tracts in the peduncles were nearly gone, as were the middle cerebellar peduncles, while the superior and inferior cerebellar peduncles were relatively well preserved. The olivocerebellar tracts stained fairly well. The roots of the cranial nerves were normal. The only changes in the myelin picture at all levels of the spinal cord consisted in degeneration of the lateral columns involving the crossed pyramidal and dorsal spinocerebellar tracts, and of the fasciculus of Türck. The anterior and posterior nerve roots were normal. In the cerebellum no myelin fibers remained in the molecular layer and only a few fragments in the granular zone, while there was a moderate diffuse paleness of the myelin staining of the medullary substance, especially of the terminal prolongations into the folia. Both optic nerves, the optic chiasm and the optic tracts were very small, and all were the seat of advanced demyelinization. In most of the sections this approached complete degeneration. Herxheimer's stain revealed practically no fat anywhere in the nervous system. What little there was was found within occasional fat granule cells in the perivascular spaces.

Axis-Cylinders: The changes in the axis-cylinders in Bielschowsky preparations were roughly parallel in degree and distribution to the changes in the myelin sheaths. Thus, in the cortex and subcortical white matter practically no axis-cylinders were stained, and those appeared as scattered fragments, strongly argentophilic, with variations in caliber, swelling and twisting. In the brain stem were many axis-cylinders, most of which showed evidence of beginning or more advanced disintegration. The spinal cord was well provided with axis-cylinders of relatively normal staining qualities. In the cerebellum nerve fibers were present only in the medullary substance and even here they were sparse and presented all the usual signs of advanced degeneration. Climbing and basket fibers around the Purkinje cells were completely wanting.

Neuroglia: Sections from all parts of the cerebral hemispheres, the basal nuclei and the cerebellum were crowded with macroglial and microglial nuclei; a lesser increase was found in the brain stem, and in the spinal cord there was no excess of these nuclei. They were either normal or showed signs of slight hyperplastic change. The neuroglial protoplasm was very little stained except in the spinal cord, where there was a slight protoplasmic hyperplasia, especially of the cells in and near the marginal glia.

In preparations stained with thionine of both gray and white matter from all parts of the central nervous system except the medulla and the spinal cord, there was a rather large number of gitter cells. These were large, irregularly rounded cells packed with granules which stained from pale to very deep blue. In some of the cells this substance was in the form of large flaky indefinite masses, while in others it appeared as small, dark discrete granules. The nuclei, often shrunken and angular, had the appearance of microglial nuclei. Frequently the cells were binucleate. Many lay in the perivascular spaces as well as in the nervous paren-

chyma, and here there was a tendency for them to be smaller and for the granules to stain more faintly. They did not stain with scarlet red or with osmic acid, nor were they impregnated with silver, but they did stain with hematoxylin after prolonged mordanting in potassium bichromate, resembling closely the lipoid inclusions of the ganglion cells stained in this manner. Further evidence of their lipoid nature was their strong staining by nile blue, most of the granules taking a dark blue color but some having a reddish tint.

The most striking feature of the neuroglia was the universal and profound glia fiber scar present in sections stained with Victoria blue, with Holzer's stain and

Fig. 8.—A glia scar from the frontal cortex. Holzer's stain.

with Mallory's phosphotungstic acid-hematoxylin methods. It was dense, orderly, isomorphic neuroglial sclerosis. While the arrangement of the fibers was looser in some places than in others, true status spongiosus was not seen. The entire substance of the cerebral hemispheres from the intima-pia to the ventricular walls was replaced by this feltwork (fig. 8). It was of almost equal density in the region of the basal nuclei and was very marked in the brain stem, decreasing somewhat at the lower levels. In the spinal cord it was less dense and was limited to the gray matter and the marginal zone of the lateral columns.

A similar dense feltwork occupied the entire cerebellum, with the Bergmann and tangential fibers interlacing at right angles (fig. 9). This was everywhere of about equal density except at the junction of the molecular with the granular

areas, where there was a narrow zone of diminished density. Neither collagen fibers nor reticulum could be stained in this scar.

In sections stained by Schaffer's hematoxylin method large numbers of neuroglia cells were seen to be laden with the same kind of hematoxylinophilic granules (lecithinoid) as were present in the ganglion cells (fig. 6).

Blood Vessels: Throughout the nervous system, varying in degree with the degree of change in the region, there was a uniform thickening of the walls of the blood vessels, especially of the smaller arteries, and some were slightly hyalinized. There was no occlusion of the lumens. Most of the perivascular spaces were

Fig. 9.—Glial sclerosis in a cerebellar folium. Note the absence of granule cells and the characteristic interweaving of the Bergmann and tangential fibers. Holzer's stain.

dilated—some enormously so. These were empty or contained few or many fat granule and small round cells. There were no plasma cells, and these infiltrations were evidently merely secondary to the process of degeneration.

Meninges: There was generalized leptomeningitis fibrosa without evidence of cellular exudation. The lateral ventricle was completely denuded of ependyma in many places; the ependyma was relatively normal elsewhere. The choroid plexus was normal.

Retina: In flat preparations of the retina a great increase of pigment was seen. It lay mostly in rounded cells and was not arranged in a communicating network.

These cells were present in large numbers at all levels of the membrane. The walls of the vessels were thickened and slightly pigmented. In cross-section the retina was seen to be reduced from one-half to one-third its normal thickness, as was the choroid. The retinal lamination was greatly disturbed, especially as regards the outer layers. The layer of rods and cones had entirely disappeared, and practically no recognizable traces of the outer nuclear and reticular layers remained. The inner nuclear layer was represented by a line of cells from one to three deep, but many of the nuclei of these cells had the appearance of glial nuclei. In a search through many sections only a few shadowy remnants of ganglion cells were found. The zone of the absent outer nuclear and rod and cone layers was occupied by

Fig. 10.—The retina, showing marked atrophy of all the layers and of the choroid and invasion of all the retinal zones by pigment cells. Hematoxylin and eosin stain.

a narrow, compact, fibrous-looking structure, and this same appearance of fibrosis was present in the layer of the nerve fibers. The pigment cell layer remained intact, though it was narrower than normal and heavily supplied with pigment. Large pigment cells, mostly discrete and rounded, were well supplied with dark brown pigment granules and occupied all parts of the retina in fairly large numbers, extending inward even to the internal limiting membrane. The retinal vessels were all very much thickened and hyalinized, and the lumens were extremely narrow and most of them appeared to be occluded. Such changes were present to about the same degree in all parts of the retina, both peripherally and toward the posterior pole.

The choroid was atrophied, compact and fibrosed. The arteries were sparse and much thickened. In the choroid the region of fibrosis stained like collagen, but in the retina it did not, the latter presumably representing proliferation by neuroglia fibers (fig. 10).

COMMENT

Usually in the brain of a person with amaurotic idiocy, whether of the Tay-Sachs or of the Vogt-Spielmeyer form, the white matter is surprisingly little affected. This fact has been commented on frequently by observers because it is seemingly counter to what might be expected from the widespread and advanced degeneration always found in the ganglion cells. Relatively few isolated cases in which there were appreciable changes of the white matter along with those of the ganglion cells have been described, notably those of Bielschowsky,[2] Savini-Castano and Savini,[3] Ostertag[4] and Globus.[5] Good résumés of the literature to date were given by both Bielschowsky and Globus. The most remarkable aspect of the case presented here consists in the profound destruction of the white matter, which had gone so far in the cerebral hemispheres as to lead to enormous compensatory hydrocephalus ex vacuo. Only one reported case closely resembles ours anatomically—that of Brodmann.[6] Clinically, his was a fairly typical case of juvenile amaurotic idiocy with symptoms beginning at 4 years and with a duration of nine years. Brodmann never had the opportunity to report this case fully, but so far as can be judged from his brief notes both the gross and the microscopic appearances were practically identical with those in the case recorded here. The weight of the brain was 450 Gm., and that of the cerebellum, 64 Gm., and there was extensive destruction of the cerebral white matter with marked hydrocephalus. Bielschowsky later examined the cerebellum in detail, and his observations corresponded closely to those made in our case.

A further striking feature in the brain of our patient was the outstanding participation of the neuroglia, first in the form of an enormous glial fibrosis and, second, in the accumulation of lecithinoid granules within the neuroglial protoplasm. Schaffer,[1] Savini-Castano and Savini,[3]

2. Bielschowsky, M.: Zur Histopathologie und Pathogenese der amaurotischen Idiotie mit besonderer Berücksichtigung der zerebellären Veränderungen, J. f. Psychol. u. Neurol. **26**:123, 1920.

3. Savini-Castano, T., and Savini, E.: Beitrag zur Aetiologie, Pathogenese und pathologischen Anatomie der Tay-Sachsschen familiären amaurotischen Idiotie, Ztschr. f. Kinderh. **7**:321, 1913.

4. Ostertag, B.: Amaurotische Idiotie mit Entwicklungsstörungen des Gehirns und Kleinhirnatrophie, Zentralbl. f. d. ges. Neurol. u. Psychiat. **39**:190, 1925.

5. Globus, J. H.: Ein Beitrag zur Histopathologie der amaurotischen Idiotie, Ztschr. f. d. ges. Neurol. u. Psychiat. **85**:424, 1923.

6. Brodmann, K.: Ein Fall familiärer Idiotie mit neuartigem anatomischen Befund, Ztschr. f. d. ges. Neurol. u. Psychiat. **10**:91, 1914.

Ostertag,[4] Schob[7] and Westphal[8] referred to marked hyperplastic changes in the neuroglia or to lipoid inclusions in these cells. Bielschowsky[2] regarded the production of glial feltwork as a purely compensatory phenomenon or as the result of metaplasia consequent to a defective glial anlage. This was purely speculative, and there seems to us to be good reason to look on this change as the expression of a simultaneous primary disease of the glia equivalent to that of the ganglion cells and having the same pathogenesis. The occurrence in the brain of our patient of intense fibrous gliosis in the region of the basal ganglions and the brain stem in the presence of a large number of fairly intact myelinated fibers without any great formation of gitter cells is evidence for this view, as is also the gorging of the neuroglia with substances microchemically similar to those in the ganglion cells. We regard this association of neuroglial disturbance and degeneration of the white matter as more than fortuitous. In all the cases reported in which there have been extensive changes in myelinated structures or gross deformities of the cerebrum or cerebellum there have also been, as in our specimens, neuroglial alterations which far exceeded the bounds of mere reactive changes. In Bielschowsky's[2] case the white matter of the hemispheres was much softened and consisted of swollen glial reticulum being replaced by fibrous glia; in Globus' first case and in that of Ostertag there was softening of the cerebral white matter with formation of fat granule cells. All of these could easily be imagined to represent an earlier stage of the sclerosis seen in the brain of our patient. It appears to us that marked involvement of the white matter in amaurotic idiocy depends not on developmental, aplastic factors but on the implication of the neuroglia in the disease itself, which interferes with the production and maintenance of myelin.

Among the recent contributors to this subject, Globus[5] and Greenfield and Holmes[9] saw in the myelin degeneration a possible relationship to Merzbacher-Pelizaeus' disease, which Spielmeyer[10] demonstrated to be a progressive degenerative process rather than a form of aplasia. However, clinically, the two states differ greatly, and anatomically none of the cases of Merzbacher-Pelizaeus' disease have shown the crucial parenchymatous changes of amaurotic idiocy. Consequently, we feel

7. Schob, F.: Zur pathologischen Anatomie der juvenilen Form der amaurotischen Idiotie, Ztschr. f. d. ges. Neurol. u. Psychiat. **10**:303, 1912.

8. Westphal, A.: Beitrag zur Lehre von der amaurotischen Idiotie, Arch. f. Psychiat. **58**:248, 1917.

9. Greenfield, J. G., and Holmes, G.: The Histology of Juvenile Amaurotic Idiocy, Brain **48**:183, 1925.

10. Spielmeyer, W.: Der anatomische Befund bei einem zweiten Fall von Pelizaeus-Merzbacherscher Krankheit, Zentralbl. f. d. ges. Neurol. u. Psychiat. **32**:203, 1923.

that the proposed relationship is spurious or, at least, that the suggestion is premature.

In this group of cases in which there were marked changes in the white matter, those of Bielschowsky, Savini-Castano and Savini and Ostertag and Globus' two cases were of the infantile form of the disease, while Brodmann's should be classed as juvenile. Thus, there is no correlation of the factor of myelin destruction with either the one or the other form of amaurotic idiocy, which are commonly accepted as fairly clearcut entities. Nor does our case in other respects fit easily into the frame of "infantile" or "juvenile." Since the time of Spielmeyer's[11] first descriptions the teaching has been, and still prevails, that two distinct forms of amaurotic idiocy exist, the infantile—Tay-Sachs—and the juvenile—Spielmeyer's—with progressive blindness, weakness and mental deterioration common to both. The infantile form is characterized by an early onset within the first six months of life, a short course with death at 18 months or thereabouts, a cherry-red spot at the macula and a clear predilection for members of the Jewish race, while the juvenile form differs in the later onset at the time of second dentition, the longer course of years, the features of retinitis pigmentosa rather than of the cherry-red spot and an incidence almost exclusively in non-Jewish persons. Anatomically the infantile form exhibits: a universal swelling of ganglion cells throughout the entire nervous system, with destruction of the intracellular fibrillary network and deposit of prelipoid substances with an affinity for hematoxylin; balloon-like swelling of the dendrites, and a remarkable sparing of axis-cylinders and extracellular neurofibrils. The histologic changes in the juvenile form are essentially the same with the difference that the alterations on the whole are less profound and are greater in some localities than in others, the intracellular deposits stain with scarlet-red and there is no huge swelling of the dendrites. It was Spielmeyer's original contention that the juvenile syndrome which he defined bore no fundamental relation to Tay-Sachs' disease, but he soon modified the strictness of this view. The literature abounds in reports of cases in which individual minutiae of the histologic picture or the clinical details do not run true to type. The present case is one in point. It is neither typically infantile nor characteristically juvenile with respect to the age of onset or the duration but is more of the infantile than of the juvenile type, while the ophthalmologic findings and the racial connection are frankly juvenile. Histologically the ubiquity of the changes

11. Spielmeyer, W.: Ueber eine besondere Form von familiärer amaurotischer Idiotie, Neurol. Centralbl. **25**:51, 1906; Klinische und anatomische Untersuchungen über eine besondere Form von familiärer amaurotischer Idiotie, in Nissl, F.: Histologische und histopathologische Arbeiten über die Grosshirnrinde, Jena, Gustav Fischer, 1908, vol. 2, p. 193.

in the ganglion cells and the staining qualities of the prelipoids are outspoken characteristics of the infantile form, yet there were no dendritic swellings and the retinal changes were such as have been described only in cases of the juvenile form of the disease.

In 1914 Bielschowsky [12] delineated a third category which he called late infantile because of the age of onset and which was distinct from other forms by the accentuation of the changes in the cerebellum, leading to cerebellar atrophy. He withdrew his original assertion that cases of this type represent a combination of amaurotic idiocy with a hereditary system degeneration of the cerebellum and now regards the cerebellar manifestations as part and parcel of the endogenous degeneration, as do most other workers who have dealt with this question. Nevertheless, Bielschowsky still considers these cases sufficiently demarcated to merit the designation of a "cerebellar group." In our case, however, while the cerebellar changes were like, and were at least as great as, those described by Bielschowsky, the damage to the cerebral hemispheres was equally striking, and this appears to have been true in Brodmann's case also. Bielschowsky has repeatedly stressed two histologic details which are presumed further to single out these cases. The first of these is the existence of a degeneration type in which the centripetal intracerebellar structures, the granule cells and the climbing and basket fibers are selectively destroyed, while the Purkinje cells and their axons persist. In our case the Purkinje cell bodies and axons were as completely demolished as were the granule cells, which was an observation made also by Globus and Bielschowsky in cases of the infantile form presenting great atrophy of the cerebellum. It is suggested that Bielschowsky's cerebellar degeneration type is only an earlier stage of the total destruction seen in our case and that the constancy of the type in his three cases may well have depended on the circumstance that these cases occurred in siblings. The second point emphasized was that the degeneration in the cerebellar peduncles was limited to the brachia conjunctiva. In our case the degeneration was mainly of the middle and inferior peduncles, and there seems to us no reason to divorce that in significance from the widespread degeneration of other fiber tracts.

For the aforementioned reasons we are of the opinion that Bielschowsky's "cerebellar group" had no validity as an independent syndrome and that in general no sharp classification of cases within the field of amaurotic idiocy is possible. Variations are numerous and the only constant is the deposition of prelipoids in the ganglion cells with resulting tumefaction and fibrillary change. In the apt words of Bielschowsky: "Den ruhenden Pol in der Flucht der Erscheinungen bildet

12. Bielschowsky, M.: Ueber spätinfantile familiären amaurotische Idiotie mit Kleinhirn Symptomen, Deutsche Ztschr. f. Nervenh. **50**:7, 1914.

einzig der Schaffersche Zellprozess und alle Fälle welche dieses Merkzeichen besitzen gehören zusammen, mögen sie symptomologisch noch so weit voneinander entfernen (The fixed pole among the ephemeral phenomena is solely a characteristic of Schaffer's cell process and all cases in which this appears belong together, no matter how much they may differ symptomatologically.)" To his "symptomatologically" we would add "anatomically." We have designated the condition in our case "late infantile" simply because it occupies a position intermediate between the infantile and the juvenile form with respect to age of onset and duration, thinking in this way to indicate its atypical nature without implying that it belonged to any special type.

That this matter of classification is not merely one of academic interest but is of practical clinical importance as well is exemplified in the clinical history of our patient. Difficulties in diagnosis of a syndrome as well known as amaurotic idiocy rarely arise, yet this case offered them for the very reason that it did not conform to any one of the commonly recognized subtypes of the disease. Perhaps the greatest hindrance to a decisive diagnosis lay in the absence of the typical macular findings. This was substituted by the retinitis pigmentosa, but the significance of this was not appreciated. The importance of retinitis pigmentosa as a diagnostic criterion for juvenile amaurotic idiocy is well recognized, and it was shown by Sjögren [13] to be pathognomonic. Rogalski [14] suggested that there might be a relationship between Tay-Sachs' disease and retinitis pigmentosa, and Kufs,[15] who regarded retinitis pigmentosa and amaurotic idiocy as heterophanotypes of the same disease process, traced transition forms between the usual macular changes of Tay-Sachs' disease and retinitis pigmentosa. The occurrence in our case of retinitis pigmentosa in association with amaurotic idiocy which, if a choice must be made, was of the infantile rather than of the juvenile type, gives strong support to Kuf's conception of the essential identity of the two conditions and lends added support to the thesis that all forms of amaurotic idiocy are fundamentally similar.

We look on the fibrous leptomeningitis in our case as simply secondary to the irritation by products of degeneration poured into the

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13. Sjögren, T.: Die juvenile amaurotische Idiotie, Lund, Berlingska Boktryckeriet, 1931.

14. Rogalski, T.: Zur Kasuistik der juvenilen Form der amaurotischen Idiotie, mit histopathologischem Befund, Arch. f. Psychiat. **47**:1195, 1910.

15. Kufs, H.: Ueber die Bedeutung der optischen Komponente der amaurotischen Idiotie in diagnostischer und erbbiologischer Beziehung und über die Existenz "spätester" Fälle bei dieser Krankheit, Ztschr. f. d. ges. Neurol. u. Psychiat. **109**:453, 1927.

subarachnoid space. In this we are in accord with Hassin [16] and not with Schob, who considered the fibrous meningitis in his case of juvenile amaurotic idiocy to be a true and independent inflammatory process. The vascular thickening was unusual. We are inclined to regard this too as a reaction to the transport of large quantities of products of lipoid degeneration along the perivascular spaces. It might also be suggested that this thickening bears some relation to the hyalinzation and obliteration of the retinal vessels so regularly seen in retinitis pigmentosa and is on the same basis.

The pathogenesis of amaurotic idiocy has long been a source of dispute and theorizing. The brain of our patient offers evidence pertinent to some points of this problem. Most contemporary writers have been in agreement that the disease is degenerative rather than developmental so far as the alterations in the ganglion cells are concerned, but it has been thought by many that when defects of white matter are present these are to be explained as being due to arrested development, that is, to aplasia in the true sense of the word. Thus, Savini-Castano and Savini concluded that in their case they were dealing with a degenerative process in an underdeveloped brain. But in our case the extreme disappearance of cerebral white matter in itself is indicative of the degenerative character of the changes, for it is inconceivable that any great part of the process could be on the basis of aplasia, considering that the child was as nearly normal as he was until 14 months of age. Brodmann's case forms an even stronger argument than ours in this direction. In his patient the symptoms did not begin before the child was 4 years of age; still there was cerebral atrophy almost equal to that in the brain of our patient. One of the chief objections to regarding the changes in the white matter as degenerative is the relative absence of fat granule cells. However, cases have been recorded in which such cells presented the outstanding glial change, notably Globus' [5] first case. If the disease is looked on as a disturbance of the trophic metabolism of the cell, as for example in Marinesco's [17] ingenious speculation on the absence of oxidizing ferments, rather than on primary damage of the conduction mechanism, this will explain the apparently normal period clinically. It is likely that the pathogenic factors are active even in the fetal period and thus lead to what might be termed acquired aplasia. What proportion of the changes are on this basis

16. Hassin, G. B.: A Study of the Histopathology of Amaurotic Family Idiocy (Infantile Type of Tay-Sachs), Arch. Neurol. & Psychiat. **12**:640 (Dec.) 1924.

17. Marinesco, G.: Contribution à l'étude anatomo-clinique et à la pathogénie de la forme tardive de l'idiotie amaurotique infantile, J. f. Psychol. u. Neurol. **31**: 210, 1925.

and what is the result of the degeneration of fully or partially developed structures cannot be decided. This must vary greatly from case to case.

CONCLUSIONS

1. Involvement of the white matter in amaurotic idiocy is a result of primary participation of the glia in the endogenous degenerative process.

2. It is not possible to separate cases of amaurotic idiocy into well defined and constant subgroups. On the other hand, all the cases taken together form a firm nosologic unit, clinically and anatomically.

3. Retinitis pigmentosa may be a feature of cases of amaurotic idiocy which otherwise clinically exhibit the characteristics of the infantile form.

4. All the retrogressive pathologic changes are the expression of an acquired degenerative process.

DISCUSSION

DR. ARTHUR H. PARMELEE: In the practice of pediatrics one encounters this type of degenerative disease, having a hereditary or familial basis. There is a tendency to try to pigeonhole diseases under names which may cause difficulty; this is illustrated in the case of amaurotic family idiocy. Confusion arises from an attempt to classify it at the same time on a pathologic, an etiologic and a clinical basis. The various descriptions of the disease are confused in the degree that they feature one or the other of these three types of classification. If one tries to classify it in a clinical way, one becomes confused about such things as the time of onset and the intensity of symptoms. If one tries to classify them etiologically, one becomes involved in the matters of race and climate and of hereditary features. When one tries to classify it from the pathologic standpoint, one looks for earmarks in each case by which to label it. It seems likely that often the pathologic changes may differ, probably depending in certain instances on the duration of the disease. For example, if a child died when this degenerative process had been going on for only a short time, say six months, the pathologic changes would differ from those in cases in which the process had been going on for two years. Our patient lived for nine months in the hospital, being fed by tube, and the clinical picture differed little at the time of death from that at the time when he entered. Nevertheless, undoubtedly the degenerative process was so pronounced that the pathologic picture was entirely different from what it would have been if the child had died a year or a year and a half before he did.

The pathologic process in this condition is also of interest to the clinical pediatrician because there are other degenerative conditions closely associated with it, for example, Niemann-Pick's disease. In this disease, characterized by a disturbance of lipoid metabolism, there are not only changes in the brain at times but changes in the reticulo-endothelial cells of the body, especially those of the spleen, liver and bone marrow. In this degenerative disease there is change due to lipoid infiltration in almost every part of the body.

What can be learned from such a study as Dr. Richter has made is that the process may be really the same though at different periods of the disease and that confusion in classification lies, somewhat at least, in the duration and intensity of the disease, although it has more or less the same etiologic background.

DR. ARTHUR WEIL: Were there any evidences of familial neurologic or ophthalmologic disease?

DR. G. B. HASSIN: There are and should be recognized not two but at least four types of amaurotic family idiocy. The most famous is the infantile Tay-Sachs type, first described in 1881. The clinical pathologic features are so well known that it is not necessary to mention details. Another type, also well known, is the juvenile type, of which H. Vogt described a large number of instances. In addition, there is a late infantile type, the Jansky-Bielschowsky type, which also gives a typical clinical and pathologic picture. The children always become sick at the same age, 3½ years, and always die at the age of 7½ years. I do not see how a student of amaurotic family idiocy, on which so much time has been spent, can ignore this type.

In addition to these three there is the adult type, which also has been ignored and which possesses certain features. The existence of the four types of amaurotic family idiocy is justified on the basis of morphologic and microchemical features, which cannot be ignored. I do not agree with many of the pathologic observations of Dr. Richter. The glial proliferation is always a secondary and not a primary process, and it is not justifiable to assume that in his cases the same lesion that destroyed the ganglion cells also affected the glial tissue. The vast degeneration of the white substance mentioned by Dr. Richter and on which he lays so much stress does not occur in every case of amaurotic family idiocy. It is a rare phenomenon, though degeneration of the white substance of single nerve fibers does occur, but in proportion to the ganglion cells destroyed. The changes vary in intensity according to the duration, as Dr. Parmelee properly pointed out. In the case studied by Dr. Parmelee and me the condition lasted three years and nine months; in that case the changes were exactly the same as those reported by Dr. Richter. The changes did not justify a diagnosis of the juvenile or late infantile type but were designated as the infantile form with a protracted course. The case of Dr. Richter, so well studied though given a different interpretation, is remarkable because it demonstrates the type of changes as they occur in the transitional types of amaurotic family idiocy, which, regardless of the time of onset, the extent and the duration, belong to one disease process. The condition in Dr. Richter's case, like that in the case recorded by Parmelee and me, is thus a transition between the infantile type of Tay and Sachs and the late infantile type of Jansky and Bielschowsky. For this reason only I consider Dr. Richter's case of importance.

DR. RICHARD RICHTER: In answer to Dr. Weil, to my knowledge there was no family history of any sort of neurologic disease or ophthalmologic disease.

In reference to Dr. Hassin's remarks, there is not much for me to say, except by way of reiteration. I did not mean to imply, of course, that there are no types within the general disease of amaurotic family idiocy. I think that both Dr. Parmelee and I were impressed more with the similarities presented in the different types than with the differences. I feel that all are different aspects of the same phenomena.

INFLUENCE OF VIOSTEROL AND PARATHYROID EXTRACT ON MINERAL METABOLISM IN OSTEOGENESIS IMPERFECTA

ARILD E. HANSEN, M.D.
MINNEAPOLIS

Although numerous investigators have concerned themselves with the problems of osteogenesis imperfecta, the underlying pathogenesis of this disease remains obscure, and all measures so far suggested for its treatment are admittedly quite ineffective. The study reported here deals primarily with the mineral exchanges of the body in this disorder, particularly as these exchanges are affected by such factors as the administration of parathyroid extract and of massive doses of vitamin D. The underlying purpose of the investigation was to gain some insight into the nature of this little understood disturbance in osseous development and to ascertain whether or not the well known chemical regulators of calcium and phosphorus metabolism are capable of influencing the course of the disease to any extent.

Osteogenesis imperfecta may be defined as a more or less distinct clinical entity characterized by extreme fragility and rarefaction of the bones and an abnormal bluish coloration of the scleras. The osseous defect is responsible for a peculiar bitemporal enlargement of the skull and for frequent fractures of the ribs and of the long bones of the extremities, which lead to multiple bizarre deformities and extreme functional disability. Although the symptoms manifest themselves at different ages (osteogenesis imperfecta, osteogenesis foetalis, osteogenesis infantilis and osteogenesis tarda) and with varying degrees of severity in different patients, the disorder is undoubtedly congenital. The descriptive term osteogenesis imperfecta, introduced by Vrolik [1] in 1854, is the most widely used designation for the disease, but numerous synonyms appear in the literature; for example, fragilitas ossium, osteoporosis congenita, malacia myeloplastica, ostitis parenchymatosa chronica, osteomalacia congenita, dystrophia periostalis, periosteal dysplasia, and Lobstein's disease.

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1. Vrolik, W.: Die Frucht des Menschen und der Säugethiere, Tabulae ad illustrandam Embryogenesis Hominis et Mammalium, Leipzig, T. O. Weigel, 1854; also, Amsterdam, G. M. P. Londonck, 1849, plate 91.

According to Dietrich,[2] who has recently reviewed the literature on osteogenesis imperfecta in a comprehensive manner, Amand first described the condition in a fetus. As early as 1788 Ekman [3] described the occurrence of frequent fractures in several members of the same family. Numerous isolated reports of cases were then published. Many of these are referred to in the extensive review made by Griffith in 1897.[4] Eddowes [5] was the first to point out the association of fragility of the bones and blue pigmentation of the scleras. Bronson [6] observed the familial tendency in the occurrence of blue sclerae and frequent fractures. Hass [7] reported finding a high incidence of cardiac disease, and Frank [8] noted the presence of circulatory changes and of lipodystrophia progressiva in families in which osteogenesis prevailed. Müller [9] described the occurrence of the disease in one of twins. Schmidt [10] and Zurhelle [11] pointed out the relationship of the early to the late types of the disease. Parrot [12] differentiated achondroplasia from fetal rickets, and Rust [13] described the condition as being different from the ordinary form of osteomalacia. Stilling [14] was among the first to study the histologic alterations characteristic of the disease, and Barker [15]

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2. Dietrich, A.: II. Angeborene Magelhaftigkeit der Knochenanbildung (Osteogenesis imperfecta), in Henke, F., and Lubarsch, O.: Handbuch der speciellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1929, vol. 9, p. 193.

3. Ekman, O. J.: Descriptio et casus aliquot osteomalciae, Upsala, J. Edman, 1788; cited by Enderlen.[32]

4. Griffith, J. P. C.: Idiopathic Osteopsathyrosis (Fragilitas Ossium) in Infancy and Childhood, Am. J. M. Sc. **113**:426, 1897.

5. Eddowes, A.: Dark Sclerotics and Fragilitas Ossium, Brit. M. J. **2**:222, 1900.

6. Bronson, E.: On Fragilitas Ossium and Its Association with Blue Sclerotics and Otosclerosis, Edinburgh M. J. **18**:240, 1917.

7. Hass, J.: Sur Kenntnis der Osteopsathyrosis idiopathica, Med. Klin. **45**:1112, 1919; cited by Dietrich.[2]

8. Frank, E. S.: Lipodystrophia progressive und Osteopsathyrosis infantilis, Ztschr. f. Kinderh. **36**:229, 1922.

9. Müller, S.: Periostale Aplasie mit Osteopsathyrosis unter dem Bilde der sogenannten fetalen Rachitis, Munich, J. F. Lehmann, 1893; cited by Schabad.[36]

10. Schmidt, M. B.: Allgemeine Pathologie und pathologische Anatomie der Knochen, Ergebn. d. allg. Path. u. path. Anat. **4**:612, 1899; cited by Schabad.[36]

11. Zurhelle, E.: Osteogenesis imperfecta bei Mutter und Kind, Ztschr. f. Geburtsh. u. Gynäk. **74**:942, 1913; cited by Dietrich.[2]

12. Parrot, M. J.: Sur la malformation achondroplasique et le dieu Phtah, Bull. Soc. Anthrop. **1**:296, 1878.

13. Rust, J. N.: Theoretisch-praktisches, Handbuch der Chirurgie, Berlin, T. C. F. Enslin, 1834, vol. 12, p. 593; cited by Schabad.[36]

14. Stilling, H.: Osteogenesis imperfecta, Virchows Arch. f. path. Anat. **115**: 357, 1889.

15. Barker, T.: On Intrauterine Fractures with an Illustrative Case, Brit. M. J. **2**:806 and 823, 1857.

determined the ash content of the bones. Bookman [16] in 1911 made the first study on mineral balance recorded.

As regards the etiology of osteogenesis imperfecta many hypotheses have been presented, but little exact information has been obtained. Conrad and Davenport [17] concluded that heredity is an important factor and maintained that the tendency to the disease appears as a dominant character. The prevailing opinion is that there is a congenital defect in the mesenchyme. According to Bauer [18] and others, the histologic picture is characterized by a deficiency in the number of osteoblasts. Weber [19] described the osseous system as consisting largely of pathologic "fiber bone," the recent callus being the only portion showing the presence of osteoclasts and of osteoblasts in normal rows.

The question of underlying etiology is not answered by an admission that there is a congenital defect in the mesenchymal tissue. More important is the consideration of what basic factor or factors are responsible for this developmental failure. Dysfunction of certain endocrine glands during the period of fetal development has been regarded by some authors as being of primary importance. Because of their known influence on the metabolism of calcium and phosphorus, the parathyroid glands have received the greatest amount of attention in the study of this condition. Bauer,[18] Dietrich [2] and Wyatt and McEachern [20] reported having observed an enlargement of these structures at autopsy. Hunter [21] found that the response of patients with osteogenesis imperfecta to the administration of parathyroid extract differed in no essential way from that of normal persons. A congenital goiter was found in one case by Nicklas.[22] Klose [23] observed the development of curvatures and atrophy of the bones and a decrease in the ash content in thymectomized dogs. Gorter [24] recently reported good therapeutic

16. Bookman, A.: The Metabolism in a Case of Idiopathc Osteopsathyrosis, Arch. Int. Med. **8**:675 (Nov.) 1911.

17. Conrad, H. S., and Davenport, C. B.: Hereditary Fragility of Bone, Bull. 14, Eugenics Record Office, Cold Spring Harbor, Long Island, N. Y., 1915.

18. Bauer, H. K.: Ueber Osteogenesis imperfecta, Deutsche. Ztschr. f. Chir. **154**:166, 1920.

19. Weber, M.: Osteogenesis Imperfecta Congenita: A Study of Its Histopathogenesis, Arch. Path. **9**:984 (May) 1930.

20. Wyatt, T. C., and McEachern, T. M.: Congenital Bone Dysplasia (Osteogenesis Imperfecta) Associated with Lesions of the Parathyroid Glands, Am. J. Dis. Child. **43**:403 (Feb.) 1932.

21. Hunter, D.: A Case of Osteogenesis Imperfecta, Lancet **1**:9, 1927.

22. Nicklas, F.: Osteogenesis Imperfecta, Beitr. z. path. Anat. u. z. allg. Path. **61**:101, 1916; cited by Dietrich.[2]

23. Klose, H.: Ueber Thymusexstirpation und ihre Folgen, Arch. f. klin. Chir. **92**:1125, 1910.

24. Gorter, E.: Treatment of Fragility of Bones with Thymus Preparation, Nederl. tijdschr. v. geneesk. **73**:2022, 1929; cited by Fairbank.[28]

results from the use of thymus gland extract, and Tauber [25] was able to produce a positive retention of calcium by the administration of thymus gland extract in two patients with congenital osteogenesis imperfecta who had previously been found to have a negative balance. Kraus [26] could find no evidence of pathologic changes in the glands of internal secretion. Frontali,[27] on the other hand, found an instance of atrophy of the thymus gland associated with this condition. The evidence favoring the theory that the etiology is glandular is, however, still far from satisfactory. In fact, it falls chiefly on the negative side.

The possibility that there may be a deficiency of the enzyme phosphatase has been suggested by Fairbank,[28] but he adduced no evidence in support of this suggestion. Kay [29] considered that some of the values for plasma phosphatase found in his case of osteogenesis imperfecta were slightly above normal. In a series of similar cases Bodansky and Jaffe [30] found no abnormality. In a recent study [31] of this aspect of the problem, I also found the activity of the plasma phosphatase in four patients to be essentially normal under ordinary conditions. The only abnormality found after extensive determinations on the fixed tissues of one of these patients, who was subsequently examined at autopsy, was the almost complete absence of the enzyme in the periosteal and subperiosteal tissues and the unusually low activity of the phosphatase in the wall of the duodenum. The probability that this finding has some etiologic significance is suggested by the fact that the essentially normal callus which develops in the bone of a patient with osteogenesis imperfecta after a fracture contains a large amount of phosphatase.

The first approach to the problem of the mineral metabolism in osteogenesis imperfecta was made in 1857 by Barker [15] who found the total ash content of bone in a case of osteogenesis imperfecta to be 33.3 per cent by weight, as against from 60 to 66 per cent, the figure for normal

25. Tauber, M.: Beitrag zum Calciumsstoffwechsel bei Osteogenesis imperfecta, Monatschr. f. Kinderh. **36**:12, 1927.

26. Kraus, E. J.: Osteogenesis imperfecta und endokrines System, Virchows Arch. f. path. Anat. **274**:37, 1929.

27. Frontali, G.: Fragilita ossea congenita e timo (contributo allo studio delle distrofie ossee in rapporto con le glandole endocrine), Riv. di. clin. pediat. **18**:257, 1920.

28. Fairbank, H. A. T.: Some Remarks on Osteogenesis Imperfecta, Proc. Roy. Soc. Med. **23**:1263, 1930.

29. Kay, H. D.: Plasma Phosphatase: II. The Enzyme in Disease Particularly in Bone Disease, J. Biol. Chem. **89**:249, 1930.

30. Bodansky, A., and Jaffe, H. L.: Significance of Clinical and Experimental Serum Phosphatase Variations: Their Osseous and Non-Osseous Origin, J. Biol. Chem. **105**:11 (May) 1934.

31. Hansen, A. E.: Phosphatase Activity of the Serum and Tissues in Osteogenesis Imperfecta, Proc. Soc. Exper. Biol. & Med. **31**:1023, 1934.

bone. Enderlen [32] said that Reynard reported having found an ash content as low as 24 per cent, while in a mild or late case observed by Enderlen the figure was 62.2 per cent. Studies on mineral balance have been made in typical cases by Schwartz and Bass,[33] Bamberg and Huldschinsky,[34] Bookman,[35] and Schabad,[36] and more recently observations have been reported by Klercker,[37] Aub and Farquharson,[38] Sindler,[39] Hunter [21] and Hassmann and Verdino.[40] Interest naturally centers chiefly around the balances for calcium and phosphorus in all these studies. Although there is no unanimity of opinion on the subject, most workers agree that there is a deficient retention both of calcium and of phosphorus. Bookman [35] reported having observed evidence of a deficient retention of both elements in a 10 week old patient. The absorption of fat and the metabolism of nitrogen, sulphur and magnesium were reported to be normal in this case. Schabad [36] likewise found evidence of deficient retention of calcium and phosphorus. He claimed that greater quantities of these elements were retained after the administration of phosphorized cod liver oil, but that even then less than the normal amounts were stored. Bamberg and Huldschinsky [34] obtained similar results but did not consider the slight increase in retention which occurred after medication to be of great significance. Schwartz and Bass [33] demonstrated the presence of a positive balance for calcium as well as for phosphorus in a 7 month old infant but concluded that the quantities retained were below normal. Klercker [37] observed no abnormality in the balances for phosphorus or magnesium but found evidence of a poor retention of calcium in a 7 month old patient. He reported that the balance was negative for chlorine but slightly positive for potassium and sodium. There was a negative calcium balance in two con-

32. Enderlen, Eugen: Zur Kenntnis der Osteopsathyrosis, Virchows Arch. f. path. Anat. **131**:223, 1893.

33. Schwartz, H., and Bass, Murray H.: Osteogenesis Imperfecta: Report of a Case with the Study of Its Metabolism, Am. J. Dis. Child. **5**:131 (Feb.) 1913.

34. Bamberg, K., and Huldschinsky, K.: Ueber angeborene Knochenbrüchigkeit, Jahrb. f. Kinderh. **78**:249, 1913.

35. Bookman, A.: The Metabolism in Osteogenesis Imperfecta, with Special Reference to Calcium, Am. J. Dis. Child. **7**:436 (June) 1914.

36. Schabad, I. A.: Der Stoffwechsel bei angeborener Knochenbrüchigkeit (Osteogenesis Imperfecta), Ztschr. f. Kinderh. **11**:230, 1914.

37. Klercker, K. O.: Zur Kenntnis des Stoffwechsels, besonders des Mineralstoffwechsels bei Osteogenesis imperfecta, Monatschr. f. Kinderh. **25**:338, 1923.

38. Aub, J. C., and Farquharson, R. F.: Studies of Calcium and Phosphorus Metabolism: XV. In Various Metabolic and Bone Diseases, J. Clin. Investigation **11**:235, 1932.

39. Sindler, Adolf: Der Stoffwechsel beim Osteogenesis imperfecta, Ztschr. f. Kinderh. **42**:85, 1926.

40. Hassmann, K., and Verdino, A.: Zur Kenntnis der Osteogenesis imperfecta, Jahrb. f. Kinderh. **140**:1, 1933.

genital cases that were studied by Tauber.[25] Sindler [39] could find no evidence of disturbance in the exchanges of minerals in a 20 day old patient with osteogenesis imperfecta. Frontali [27] believed the calcium balance to be normal. Aub and Farquharson [38] found a slightly negative calcium balance in a 14 year old patient on a diet low in calcium. On roentgen examinations no evidence of improvement in the bones was seen after an adequate amount of calcium and vitamin D had been added to the diet.

Fairly extensive studies on the constituents of the blood have contributed comparatively little toward a better understanding of the pathogenesis of osteogenesis imperfecta. Kramer, Tisdall and Howland [41] and Hunter [21] reported having found normal values for the serum calcium and phosphorus. Flagstad, Zanger and Leven [42] found the values for uric acid, creatinine, urea and total nitrogen, as well as those for calcium and phosphorus, to be within normal limits. Holler [43] also reported the figures for the blood calcium to be within the normal range. Aub and Farquharson [38] and Hassmann and Verdino,[40] on the other hand, found the values for the latter two elements of the serum to be slightly elevated and Babonniex [44] reported finding a calcium content of 15.4 mg. per hundred cubic centimeters in an 11 month old patient. Ferri [45] found that in a 4 month old child with osteogenesis imperfecta the cerebrospinal fluid contained less calcium than normal, but the content returned to normal after sunlight therapy. Mensi [46] stressed the fact that the possible association of rickets in young patients caused the findings to be complicated. Benjamin and Hess [47] in a study on the adsorbable fractions of the blood calcium and phosphorus, found the total calcium, the protein-bound calcium, the adsorbable complex—total filtrable and nonfiltrable fractions—and the ionized fraction to be essentially normal, as were the total adsorbable and ionized complexes of phosphorus.

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41. Kramer, B.; Tisdall, F. F., and Howland, J.: The Clinical Significance of Calcium Concentration in the Serum of Children and Possible Errors of Its Determination, Am. J. Dis. Child. **22**:560 (Dec.) 1921.

42. Flagstad, A. E.; Zanger, E., and Leven, L.: Blood Chemistry Study in Osteogenesis Imperfecta; Preliminary Report, Minnesota Med. **7**:800, 1924.

43. Holler: Zur Frage des Kalkstoffwechsels bei Fällen von Osteopsathyrosis idiopathica, Verhandl. d. deutsch. orthop. Gesellsch. **20**:273, 1925.

44. Babonniex, L.; Ducroquet, R., and Wilm: Maladie de Lobstein, Bull. Soc. de pédiat. de Paris **30**:437 (July) 1932.

45. Ferri, U.: Un caso di fragilita congenita delle ossa, Pediatria **33**:20, 1925.

46. Mensi, E.: Sulla diagnosi differenziale del rachitismo e dell' osteopsatirosi, Clin. e ig. inf. **5**:185, 1930; Zentralbl. f. d. ges. Kinderh. **24**:547, 1930.

47. Benjamin, H. R., and Hess, A. F.: The Forms of the Calcium and Inorganic Phosphorus in Humans and Animal Sera: I. Normal, Rachitic, Hypercalcemia, and Other Conditions, J. Biol. Chem. **100**:27, 1933.

The lack of uniformity in the results of the various studies thus far made is probably explainable on the basis of differences in the stages of the disease or in the types of cases studied. Some of the earlier results from studies on metabolic balance cannot be relied on because of certain fundamental objections such as too short experimental periods, the presence of complicating clinical disturbances and inadequate control of the various dietary factors. For instance, as regards the latter, it is obvious that the vitamin content, the ratio of calcium to phosphorus and the acid-base balance of the diet were not recognized as being important factors.

In regard to the therapy of osteogenesis imperfecta it is readily admitted by the vast majority of observers that no definite progress has thus far been made. High intake of calcium and phosphorus in the diet appears to have little influence on the bones. Ordinary antirachitic therapy is without avail even after three years of trial.[38] Dietrich,[48] however, found histologic evidence of the formation of new bone in the periostium in a 10½ month old child with osteogenesis imperfecta who had been treated from birth with viosterol. The results which Hunter [21] observed after the administration of parathyroid extract point to no direct benefit from this form of treatment.

While viosterol administered in ordinary therapeutic doses was found by Hassmann and Verdino [40] to cause no increase in the retention of calcium and phosporus in patients with osteogenesis imperfecta, it is well known that in normal persons this substance influences mineral metabolism differently when given in very large doses and when given in ordinary antirachitic doses. In fact, Taylor, Weld, Branion and Kay [49] have gathered a great deal of evidence, based on pathologic findings, individual physiologic responses and species reactivity, which indicates that large doses of viosterol and parathyroid extract exert essentially the same influence on the animal economy. They, as well as Hess and Lewis,[50] contended that viosterol acts through the medium of the parathyroid glands. Thus far no attempt has been made to determine the effects of massive doses of viosterol on the mineral exchanges or on the clinical course of osteogenesis imperfecta. Since this disease has certain features which suggest a disturbed activity of the parathyroid

48. Dietrich, A.: Angeborene Knochenbrüchigkeit (Osteogenesis Imperfekta) mit Besserung (durch Vigantol?), Virchows Arch. f. path. Anat. **275**:398, 1929.

49. Taylor, N. B.; Weld, C. B.; Branion, H. D., and Kay, H. D.: A Study of the Action of Irradiated Ergosterol and of Its Relationship to Parathyroid Function, Canad. M. A. J. **24**:763, 1931; **25**:20, 1931.

50. Hess, A. F., and Lewis, J. M.: Clinical Experience with Irradiated Ergosterol, J. A. M. A. **91**:783 (Sept. 15) 1928.

glands, it seemed of importance to determine whether or not either of the aforementioned agents would accentuate or ameliorate such a tendency, if present. The present study was undertaken in part with this objective in view.

METHODS AND MATERIALS USED

The plan of study as finally carried out involved the quantitative determination of the amount of calcium, phosphorus, magnesium, potassium, sodium, sulphur, chlorine and nitrogen in the urine and feces in two typical cases of osteogenesis imperfecta over several months, during which the patients were given basic diets of known composition. The time of observation was divided into a preliminary control phase and two main experimental phases, with a control interval between the latter. Except for the administration of viosterol during the first experimental phase and of parathyroid extract during the second, all conditions remained constant for the entire duration of the study.

The patients were kept in the special metabolism ward under the constant supervision of graduate nurses. They were placed in suitable mechanical frames to insure accurate quantitative collection of specimens. The temperature and humidity of the room were ideally adjusted to prevent loss of minerals by way of the skin from sweating.

The food was prepared in the pediatric nutrition laboratory under the supervision of the dietetic department. Special care was taken in the selection of the articles of diet in order to make them complete as regards known nutritional requirements. The diets were calculated so as to contain sufficient calories to prevent loss of weight and sufficient protein to maintain a slightly positive nitrogen balance. A preliminary time of adjustment of nearly two weeks before the study proper was begun showed the diet to be satisfactory in these respects. Particular attention was given to the calcium and phosphorus contents and to the ratio of these two elements to each other. For one of the patients, A. O., the daily intake was 0.783 Gm. of calcium and 0.881 Gm. of phosphorus, and the ratio of calcium to phosphorus, 1 : 1.12. This provided 0.031 Gm. of calcium and 0.035 Gm. of phosphorus per kilogram of body weight per day. For the second patient, D. J., the daily intake of calcium was 0.583 Gm., and that of phosphorus, 0.670 Gm.; the ratio of calcium to phosphorus was 1 : 1.15, and the absolute intake, 0.058 Gm. of calcium and 0.064 Gm. of phosphorus per kilogram of body weight per day. While the calcium-phosphorus ratio was essentially the same for the two patients, the intake per unit of body weight for the second patient was approximately double that for the first.

The diet was composed of powdered milk (Klim), white of egg, yolk of egg, and cane sugar. Sodium chloride and water were added to suit the requirements. Vitamin supplements in the form of lemon juice, cod liver oil and powdered yeast were used. The powdered milk, egg white and egg yolk and some of the sugar, sodium chloride and water were used to make a formula, and lemon juice and sugar were served as lemonade. The cod liver oil and yeast were served separately with the meals. The meals, which were served at 7 a. m., 12 noon and 6 p. m., were identical, each containing one third of the total allowance for the day. Any food that was refused was carefully weighed, and a record of the type and amount was kept by both the nurse in charge and the dietitian. Drinking

water was given as desired. The diet for A. O. (case 1) is given in detail in table 1. It was composed of the following ingredients: egg yolk, 66 Gm.; egg white, 66 Gm.; powdered whole milk, 81 Gm.; cane sugar, 99 Gm.; lemon juice, 42 Gm.; cod liver oil, 9 Gm.; yeast, 2 Gm., and sodium chloride, 3 Gm.

The diet for D. J. (case 2) was made up in the same manner as that for A. O., the only difference being that somewhat smaller quantities of egg, milk and sugar were used. The essential data are summarized in table 2.

The urine was collected in three day periods. The specimen voided at 7 a. m. on the first day was discarded; then all the specimens were collected up to and including the specimen voided at 7 a. m. on the third day. After being measured, the specimens of urine were preserved with acetic acid and toluene and stored in a dark, cool cupboard until analyses could be made. Stools were marked by

TABLE 1.—*Essential Constituents of Daily Diet Given to A. O. (Case 1)* *

Protein	Fat	Carbohydrate	Water
41.5	53.5	135	900

Mineral Content†						
Calcium	Phosphorus	Magnesium	Potassium	Sodium	Chlorine	Sulphur
0.783	0.881	0.091	1.180	1.609	2.651	0.392

* The amounts are given in grams; the diet was calculated so as to contain 1,220 calories.
† The excess of acid over base equaled 94 cc. of tenth-normal hydrochloric acid.

TABLE 2.—*Essential Constituents of Daily Diet Given to D. J. (Case 2)* *

Protein	Fat	Carbohydrate	Water
31.59	42.65	101.53	1,200

Mineral Content†						
Calcium	Phosphorus	Magnesium	Potassium	Sodium	Chlorine	Sulphur
0.583	0.671	0.068	2.664	2.734	4.592	0.301

* The amounts given are in grams; the diet was calculated so as to contain 971 calories.
† The excess of acid over base equaled 77 cc. of tenth-normal hydrochloric acid.

means of carmine given orally in doses of 0.2 Gm. at the beginning of each period. The colored stool appeared usually in from thirty-six to forty-eight hours. Because of the rather great discrepancy in the size of the stools collected in three days, often the feces were combined into one or more large specimens, and the average was calculated for each individual three day period. This was done only when the conditions were uniform throughout the period. The stools were weighed and dried on a water bath to constant weight for analyses. The following methods of analysis were used: calcium, that of Van Slyke and Sendroy;[51] for phosphorus, that of Fiske and Subbarrow;[52] for potassium, that of Shohl and Bennett;[53] for

51. Van Slyke, D. D., and Sendroy, J., Jr.: Gasometric Determination of Oxalic Acid and Calcium and Its Application to Serum Analysis, J. Biol. Chem. **84**:217, 1929.

52. Fiske, C. H., and Subbarow, Y.: The Calorimetric Determination of Phosphorus, J. Biol. Chem. **66**:375, 1925.

53. Shohl, A. T., and Bennett, H. B.: A Micro Method for the Determination of Potassium as Iodoplatinate, J. Biol. Chem. **78**:643, 1928.

sodium, that of Barber and Kolthoff ; [54] for magnesium, that of Fiske and Logan ; [55] for chloride, that of Volhardt and Arnold ; [56] for sulphur, that of Fiske,[57] and for total nitrogen, that of Kjeldahl and Sorenson.[58]

Throughout the course of the study periodic clinical examinations, routine examinations of the blood and urine, roentgenograms and determinations of the amount of minerals and phosphatase in the blood were made in addition to the studies of the mineral balance. Results of the studies on the mineral content of the blood are not reported here.

Fig. 1 (case 1).—Osteogenesis imperfecta as seen in A. O., aged 12 years.

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54. Barber, H. H., and Kolthoff, I. M.: A Specific Reagent for the Rapid Gravimetric Determination of Sodium, J. Am. Chem. Soc. **50**:1625, 1928.

55. Fiske, C. H., and Logan, M. A.: The Determination of Magnesium, unpublished data.

56. Volhard-Arnold Method for Chlorides, in Hawk, Philip B., and Bergeim, Olaf: Practical Physiological Chemistry, Philadelphia, P. Blakiston's Son & Co., 1931, p. 879.

57. Fiske, C. H.: The Determination of Inorganic Sulfate, Total Sulfate and Total Sulfur in Urine by the Benzidine Method, J. Biol. Chem. **47**:59, 1921.

58. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins Company, 1932, p. 534.

For determining the effects of viosterol, viosterol 250 D was given in doses of 8 cc. daily for nine days in each case, after which viosterol 10,000D was given in graduated doses of from 0.1 cc. to 0.5 cc. daily for twenty-four days.[58a] This dosage was two and one-half times greater per unit of body weight for D. J. (case 2) than for A. O. (case 1). After this thirty-three day course of treatment and after an intervening rest of one month A. O. was given 0.5 cc. of viosterol 10,000D daily for fifteen days in addition to the first course. This daily dosage provided a vitamin D content equivalent to that of 5 liters of cod liver oil. During the second experimental phase parathyroid extract was administered to both patients for nine days. The latter medicament was given subcutaneously to each patient in doses of 20 units per day. The dose per unit of body weight was, therefore, much greater in the case of D. J. than in that of A. O.

REPORT OF CASES

The report of the cases of the two patients used in the study is as follows:

CASE 1.—A. O., a girl aged 12 years, was admitted to the University Hospitals on Jan. 30, 1930, with the complaint of complete invalidism due to the occurrence of frequent fractures. The mother stated that at the age of 16 months the child had sustained a fracture of the right humerus from a slight injury. Two more fractures of the right humerus occurred during the following year; then one of the right femur took place. These fractures occurred on such slight provocation as falling from a standing to a sitting position or bumping a leg against a table or chair. Up to the time of admission the patient had sustained about sixty known fractures and had acquired multiple deformities, particularly of the arms and legs. The mental development was subnormal, although the patient was cheerful and cooperative. She was a full term child. Delivery had been normal. She was breast fed up to the age of 7 months. At the age of 1 year she was seen in the outpatient clinic of the University Hospitals where, because of an apparent enlargement of the head, a diagnosis of possible hydrocephalus was made. At the age of 3 she was admitted to the State Hospital for Crippled and Indigent Children where the attending physician noted that her sclerae were dark blue. There was no familial tendency to frequent fractures or blue sclerae.

On physical examination the patient presented a striking appearance because of the marked deformities of the trunk and extremities. The rather large head, deformed chest and protruding abdomen together with the markedly twisted extremities presented a pathetic picture. There were no tumor masses in the region of the thyroid gland. There was a slight bilateral temporal prominence of the head and the forehead was somewhat protruding. The hair had a fine texture and was rather sparse. The sclerae had a slightly bluish tinge. The reactions of the pupils, the visual fields and the retinas were normal. There were no defects in the auditory apparatus. The enamel of the teeth was grooved and atrophic, and several carious foci were present. The chest was markedly deformed and unusually prominent anteriorly. No abnormalities were demonstrable in the heart or lungs. The abdomen was prominent. Because of the formation of pseudojoints in the elbows, the arms were extremely mobile in all directions. The fingers were long and narrow, and the muscular power was feeble. The lower extremities had marked angulations just above the ankle joints. Scoliosis was present, and the entire trunk was shortened. The weight was 25 Kg. The pulse rate, temperature and respiratory rate were normal.

58a. The viosterol was made available by the Mead Johnson Co.

The routine laboratory examinations gave the following results: The hemoglobin was 78 per cent; there were 3,770,000 erythrocytes and 12,500 leukocytes per cubic millimeter. The differential count showed 74 per cent polymorphonuclears, 24 per cent lymphocytes and 2 per cent large mononuclears. The urine was essentially normal. The results of the chemical analysis of the blood were as follows: calcium, 12.1 mg. per hundred cubic centimeters of serum; phosphorus, 4.2 mg.; phosphatase, 0.1215 units per hundred cubic centimeters of plasma (Kay's [59] method). The values for the protein and the nonprotein nitrogen content of the serum were normal. Specimens of the stool were negative for occult

Fig. 2 (case 2).—Osteogenesis imperfecta as seen in D. J., aged 3 years.

blood and contained no ova or parasites. The Wassermann test of the blood was negative. Tests with tuberculin and the Schick test were also negative. The roentgen examination revealed evidence of multiple old fractures of the bones of the legs, pelvis and arms and extreme deformities. The cortex of the bone appeared very thin, and there was considerable decalcification, the trabeculations being rather coarse. Some of the fractures showed formation of callus. The bones of the hand were unusually long. The deformity of the right arm was most extreme, and there was evidence of dislocation of the elbow. The skull showed

59. Kay, H. D.: Plasma Phosphatase: I. Method of Determination; Some Properties of Enzyme, J. Biol. Chem. **89**:235, 1930.

slight decalcification but no other evidence of pathologic changes. There were also marked deformity of the spine and multiple fractures of the ribs. There was marked anterior bowing of the right tibia and fibula, and sharp angulation was noted medially at the distal ends of both legs.

CASE 2.—D. J., a girl aged 3 years, was admitted to the University Hospitals on Nov. 20, 1930, with the complaint of frequent fractures occurring on slight provocation and causing her continuous confinement to bed. When the child was 1½ years of age, while holding onto a chair, she fell from a standing to a sitting position and sustained a fracture of the left femur. A little later she again suffered a fracture of the left femur. The fractures healed in about six weeks. It was noted shortly after the patient's birth that she was rather small and that the extremities were rather short. The legs showed slight anterior bowing. She was breast fed up to 7 months of age and given cod liver oil and orange juice. She made no attempt to talk until she was 18 months old. She began to crawl at about that time. There was no known familial tendency to blue pigmentation of the sclerae or to frequent fractures.

On physical examination the child presented a striking and rather characteristic appearance because of the marked steel-blue sclerae and the peculiar bowing and atrophic condition of the legs. She was quiet and cooperative. The measurements were: length, 66 cm.; circumference of the head, 49.5 cm.; circumference of the chest, 45.5 cm., and circumference of the abdomen, 43 cm. The weight was 10 Kg. The frontal and occipital regions of the head were prominent, and the cranial vault was somewhat flattened. The hair was fine but rather abundant. Aside from the dark, steel-blue sclerae, the eyes were normal. There was no difficulty in hearing. The teeth were in good condition. The thoracic cage was short and broad and exhibited undue prominence of the sternal region. There were no palpable masses along the ribs. The heart and lungs were normal. The abdomen was not unduly enlarged. The lower extremities were small and flabby; the thighs were short and markedly bowed; the legs curved anteriorly, and the feet were small. The upper extremities appeared normal except for a slight shortening. The fingers were small and delicate. The trunk was rather short and showed some kyphosis and a slight scoliosis to the left. The temperature, pulse rate and respiratory rate were normal.

The routine laboratory examination gave the following results: The hemoglobin was 72 per cent; there were 3,850,000 erythrocytes and 7,750 leukocytes per cubic millimeter. The differential count showed 55 per cent polymorphonuclears, 41 per cent lymphocytes, 2 per cent large mononuclears and 2 per cent eosinophils. The specimens of the urine and stool were normal. The amounts of calcium and phosphorus in the serum were 10.7 and 4.8 mg. per hundred cubic centimeters, respectively. The phosphatase content of the plasma was 0.1222 units per hundred cubic centimeters. The values for the protein and the nonprotein nitrogen content of the serum were normal. An analysis of 22 cc. of gastric contents yielded: free hydrochloric acid, 19, and total acid, 41. The Wassermann and the tuberculin tests were negative. The Schick test was positive. The roentgen examination disclosed extreme osteoporosis of all the bones of the pelvis and spine and of the long bones. The cortex of the bones appeared to be very thin. The bodies of the vertebrae were thin and almost disklike in appearance because of the extreme decalcification. The femurs and the tibias were markedly bowed. There was an old fracture in the middle of the shaft of the left femur which had a fairly large amount of callus formation.

RESULTS

The results are presented in four subdivisions as follows:

1. Mineral balance during the control phase. The observations in case 1 for this division are represented in figure 3 (periods 1 to 7). Those in case 2 are shown in figure 4 (periods 2 to 11).

2. Mineral balance as affected by the administration of viosterol. The results for case 1 are shown in figure 3. The first course of administration of viosterol comprises periods 8 to 18, and the second includes periods 31 to 35. Periods 36 to 40 indicate the mineral exchange occurring after the withdrawal of viosterol. The results in case 2 are shown in figure 4. The course of administration of viosterol comprises periods 12 to 22, and periods 23 to 28 represent the mineral exchange in the interval following the use of this substance.

3. Mineral balance as affected by administration of parathyroid extract. The results for both case 1 and case 2 are presented in figure 5. The results of observation in the nine days during which the parathyroid extract was administered are shown in periods 25 to 27 for case 1 and in periods 29 to 31 for case 2. The results during the interval of rest following the use of parathyroid extract are shown in the three succeeding periods in each case.

4. Influence of viosterol and parathyroid extract on the plasma phosphatase. The results are summarized in table 6.

Mineral Balance During the Control Phase.—As indicated in chart 1, A. O. showed a small storage of calcium throughout the control phase. On the other hand, there was a slightly negative balance for phosphorus, magnesium and sulphur. All the remaining elements were retained to a slight degree. The results in D. J. varied little from those in A. O. except for a slightly positive balance for phosphorus and sulphur. These differences between the two patients, however, fall within the range of error of the methods employed. The lack of opportunity to conduct control studies on the mineral balance in normal children necessitates comparison with data obtained by other workers on normal persons.

Carefully controlled studies on calcium retention in normal children have recently been made by Sherman and Hawley [60] and by Stearns.[61] The former found that in children from 3 to 13 years the average daily storage was 0.010 Gm. of calcium per kilogram of body weight. Stearns, from an extensive study of the calcium metabolism in children, found values of the same magnitude. In a study on 6 boys ranging in age from

60. Sherman, H. C., and Hawley, E.: Calcium and Phosphorus Metabolism in Childhood, J. Biol. Chem. **53**:375, 1922.

61. Stearns, G.: The Retention of Calcium from Early Infancy to Adolescence, J. Biol. Chem. **105**:LXXXIV (May) 1934.

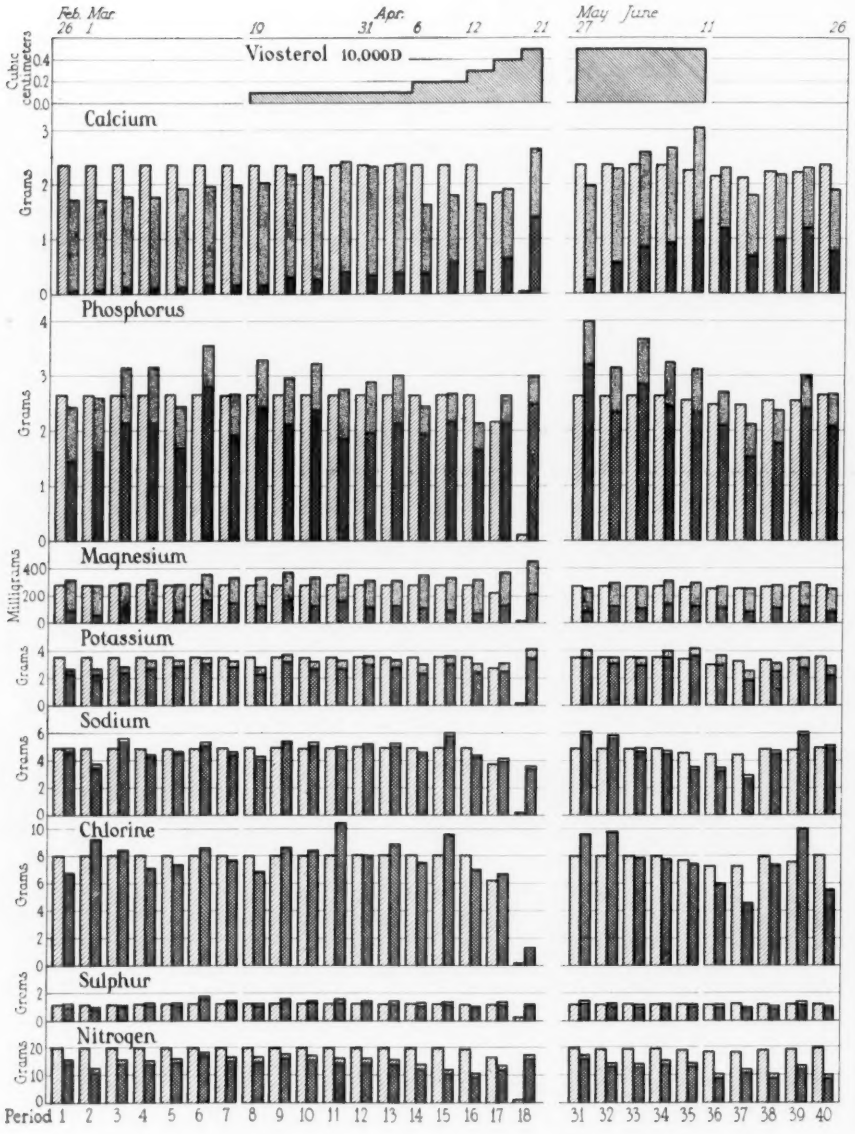

Fig. 3 (case 1).—Effect of massive doses of viosterol on the mineral balances. The diagonal lines indicate intake of the respective substances; the cross-hatching, urinary ouput, and the stippling, fecal output.

6 to 14 years, Herbst [62] found that the amount of calcium stored daily was from 0.01 to 0.016 Gm. per kilogram of body weight. The intake of 0.783 Gm. of calcium per day in case 1, especially since the chief source was milk and since cod liver oil was included in the diet, should have been adequate for normal retention. In the twenty-one day control

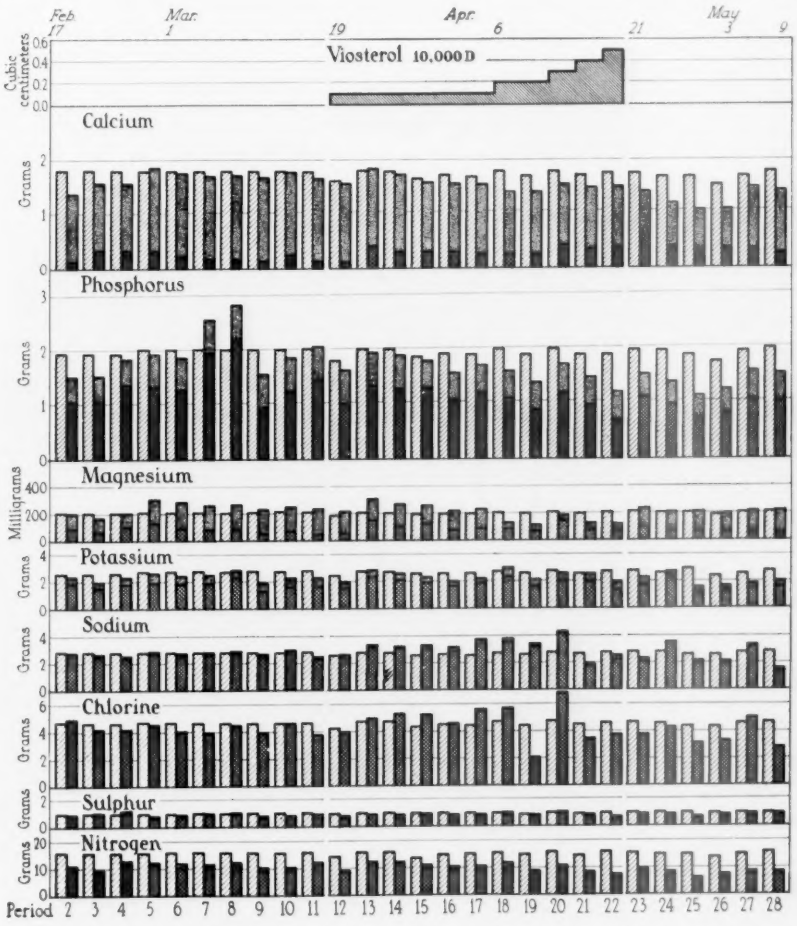

Fig. 4 (case 2).—Effect of massive doses of viosterol on the mineral balances. The diagonal lines indicate intake of the respective substances; the cross-hatching, urinary output, and the stippling, fecal ouput.

phase there was an average daily retention of 0.164 Gm. of calcium, or 0.0065 Gm. per kilogram, in case 1. The normal retention in this case should have been 0.25 Gm. per day. In case 2 the intake of

62. Herbst, O.: Beiträge zur Physiologie des Stoffwechsels im Knabenalter mit besonderer Berücksichtigung einiger Mineralstoffe, Jahrb. f. Kinderh. **76**:40, 1912.

calcium was 0.583 Gm. per day, and the retention, 0.042 Gm., was definitely less than the expected retention of 0.1 Gm. per day for a normal child. These findings indicate that there is a deficient retention of calcium in cases of osteogenesis imperfecta.

The phosphorus requirement for the growing child has not been as thoroughly studied as that of calcium. Sherman and Hawley [60] stated that the amount of phosphorus required daily by a normal child is 0.008 Gm. per kilogram of body weight. In case 1 the phosphorus balance was negative. While the ideal ratio of calcium to phosphorus for maximum retention is 1:1.5, the ratio in the diet described was 1:1.12. In case 2 the amount of phosphorus retained daily was only 0.007 Gm., or 0.0007 Gm. per kilogram of body weight in the thirty day experimental phase of the study. The ratio of calcium to phosphorus in this case was 1:1.15. The expected retention for a normal child of the same age and weight as D. J. is 0.080 Gm. of phosphorus per day. The deficiency in retention was more marked in the case of phosphorus than in that of calcium.

It is well known that magnesium salts may exert considerable effect on the calcium metabolism. In this experimental study it was found that for both patients the intake of magnesium was relatively low. The slightly negative balance for magnesium that existed in both cases is of questionable significance. In both case 1 and case 2 there was a positive balance for potassium of 0.165 Gm. and 0.111 Gm., respectively. The positive balance for sodium 0.062 Gm. in case 1 and 0.004 Gm. in case 2) was near to equilibrium. The chlorine balance was slightly positive in both cases. The fact that there was only a slightly positive balance for potassium, sodium and chlorine indicates that no particularly large amount of these elements had been lost through the skin. In case 1 the sulphur balance was slightly negative, and in case 2 it was positive, but in neither case was the variation striking. The nitrogen balance was positive in both cases, indicating that no destruction of body protein took place during this preliminary control phase.

Mineral Balance as Affected by the Administration of Viosterol.—When large doses of viosterol were given in case 1 (fig. 3, periods 8 to 18) there was a definite decrease in the calcium balance, and this decrease became more marked when the larger doses were administered. The negative balance in the second course of administration of viosterol, periods 31 to 35, amounted to 0.053 Gm. of calcium per day. The same phenomenon was observed in case 2 (fig. 4), periods 12 to 22. The values for calcium retention in periods 12, 13 and 14 were negative. In periods 15, 16 and 17 the intake and output were nearly equal. When the doses of viosterol were increased in periods 18, 19, 20, 21 and 22 the balance became positive. The average daily retention for the thirty-three day course in case 2 was not greatly different from the retention

in the control interval. The dose of viosterol per unit of weight administered to this patient was two and one-half times that used in case 1. The urinary output of calcium was definitely increased in all the periods during the administration of viosterol. In case 1, period 17, the urinary output of calcium was nearly three times as great as in the control interval, and in period 18 it was from six to seven times greater. During the second course of administration of viosterol (periods 31 to 35) the increase in the urinary calcium was even more marked. In case 2 the increase in the urinary calcium was not as striking. In both cases the fecal calcium was definitely decreased in all the periods in which viosterol was administered. The marked increase in the urinary output and the decrease in the fecal output of calcium continued in the interval following the administration of viosterol in case 1 (periods 36 to 40). The balance, however, was slightly positive. The same changes were present in the interval following the administration of viosterol in case 2 (periods 23 to 28).

The effect of administration of viosterol on the phosphorus exchange was similar to that on calcium. In case 1 (fig. 3) there was a striking decrease in phosphorus retention. In case 2 (fig. 4) the changes in the phosphorus balance were similar to those of the calcium balance, both balances showing a slight tendency to increase with the increasing doses of viosterol. The urinary phosphorus first increased and later decreased in each instance. The fecal phosphorus was slightly increased in case 1 in the first course of administration of viosterol, but was definitely decreased in the second fifteen day course (periods 31 to 35). In case 2 there was a tendency toward a diminution in the fecal output of phosphorus. In the control interval following the administration of viosterol in case 1, the negative balance for phosphorus and the decreased fecal output continued. In the corresponding interval in case 2 the fecal phosphorus decreased; later the urinary phosphorus decreased and the balance became slightly more positive.

No reference relative to the effect of large doses of viosterol either on normal children or on patients with osteogenesis imperfecta could be found in the literature. Bauer, Marble and Claflin [63] recently reported the results of their study of the effect of various doses of viosterol on normal adult persons. These workers and Harvard and Anderson [64] were not able to demonstrate any effect on the metabolism of calcium and phosphorus in normal adult persons when viosterol was given in ordinary therapeutic doses. The changes found in the calcium

63. Bauer, W.; Marble, A., and Claflin, D.: Studies on the Mode of Action of Irradiated Ergosterol: I. Its Effect on the Calcium, Phosphorus and Nitrogen Metabolism of Normal Individuals, J. Clin. Investigation **11**:1, 1932.

64. Havard, R. E., and Anderson, R. J.: Vitamine D in Adults, Its Affect on the Calcium and Inorganic Phoshorus of Blood, Biochem. J. **22**:713, 1928.

and phosphorus balances by Bauer and his co-workers when large doses of viosterol (30 mg. daily) were administered to normal persons together with the changes observed in this study have been summarized in table 3.

From table 3 it is evident that the effect of viosterol in patients with osteogenesis imperfecta differs from the effect in normal persons. The balances for calcium and phosphorus become fairly strongly negative in patients with osteogenesis imperfecta, but they are scarcely affected in normal subjects. In normal subjects the urinary phosphorus first decreases and then increases, while the opposite reaction is seen in patients with osteogenesis imperfecta; namely, there is an increase followed by a decrease. Bauer and his co-workers [63] found that after the adminis-

TABLE 3.—*Comparison of the Effect of Large Doses of Viosterol on the Balances for Calcium and Phosphorus in Normal Persons and in Patients with Osteogenesis Imperfecta*

	Normal Persons (Bauer et al.[63])	Patients with Osteogenesis Imperfecta
Urinary output	Calcium, slight decrease followed by increase	Calcium, marked increase
	Phosphorus, slight decrease followed by increase	Phosphorus, slight increase followed by slight decrease
Fecal output	Calcium, immediate increase followed by decrease	Calcium, decrease
	Phosphorus, immediate increase followed by slight decrease	Phosphorus, tendency to decrease
Total balance	Calcium, unchanged	Calcium, definitely negative
	Phosphorus, unchanged	Phosphorus, usually negative but at times slightly increased

tration of viosterol to normal persons was discontinued the values for fecal calcium and phosphorus rose promptly and those for the urinary output of these elements fell slightly. As already noted, a quite different reaction was observed in patients with osteogenesis imperfecta. The value for urinary calcium remained elevated for at least fifteen days. The value for urinary phosphorus fell for a short interval and then returned to the former level in from seven to ten days. The fecal output of both calcium and phosphorus decreased. These findings suggest that viosterol has a more sustained effect in osteogenesis imperfecta.

The magnesium balance was not influenced to any degree by the administration of viosterol. Withdrawal of the drug produced no change worthy of note. The potassium balance decreased in all the periods studied, as shown in figures 3 and 4. In the interval following the withdrawal there was no evidence of an increase. The urinary sodium definitely increased during the course of administration of viosterol (case 1, fig. 3, and in case 2, fig. 4). The urinary chlorides also increased in both cases. The sodium balance increased slightly, and the chlorine balance increased definitely in the intervals following

the administration of viosterol. The sulphur balance was not changed to any significant degree. There was a slight decrease in the nitrogen balance during and a slight increase after administration of viosterol. Bauer, Marble and Claflin found no change in the nitrogen metabolism in normal adult persons when viosterol was administered.

Mineral Balance as Affected by Administration of Parathyroid Extract.—The data presented in figure 5 show the influence of parathyroid extract on the complete mineral exchange in patients with osteogenesis imperfecta. The most striking feature of the results as observed in both case 1 and case 2 was the enormous increase in the urinary and fecal calcium. The negative balance in case 1, for example, amounted to a daily loss of 0.474 Gm. of calcium. The change observed after withdrawal of the parathyroid extract in this experiment was identical with that seen in the normal person under similar conditions; namely, there was a marked increase in the calcium retention due to a decrease in both the urinary and the fecal output. As regards the effect of the hormone on the phosphorus balance, it may be noted that there was a transient, slight decrease followed by a gradual increase in the urinary phosphorus. The fecal phosphorus was definitely increased during administration of parathyroid extract. As shown by a comparison of the data in figure 5, the increase in fecal phosphorus as a result of the administration of parathyroid extract was much greater in A. O. (case 1) than in the younger patient, D. J. (case 2). In the interval following the administration of parathyroid extract there was a sustained drop in the fecal phosphorus. There was a decided decrease in the urinary phosphorus also during the first three days following the cessation of medication with parathyroid extract, but the value soon returned to the former level. The effects of parathyroid extract on the balances for calcium and phosphorus obtained in this study are summarized in table 4 and are there compared with the changes noted by Albright, Bauer, Ropes and Aub [65] in normal persons.

From the summary presented in table 4 it is seen that the reactions of calcium, namely, an increased urinary and fecal output, resulting in a negative balance, are the same in patients with osteogenesis imperfecta as in normal persons. The effect on the phosphorus exchange, however, appears to be different, particularly as manifested in the urinary output; in patients with osteogenesis imperfecta this decreases at first and later increases. In normal persons the urinary phosphorus tends at first to increase and later may fall. The fecal phosphorus is usually increased in patients with osteogenesis imperfecta, while no change occurs in normal

65. Albright, E.; Bauer, W.; Ropes, M., and Aub, J. C.: Studies of Calcium and Phosphorus Metabolism: IV. The Effects of the Parathyroid Hormone, J. Clin. Investigation **7**:139, 1929.

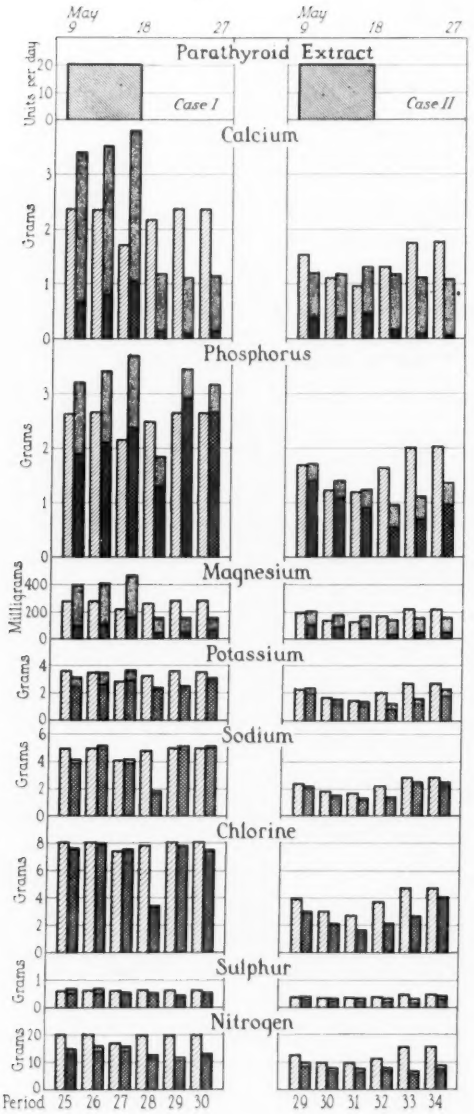

Fig. 5.—Effect of subcutaneous administration of parathyroid extract on the mineral balances in A. O. and D. J. The diagonal lines indicate intake of the respective substances; the cross-hatching, urinary output, and the stippling, fecal output.

persons. The total phosphorus balance is usually negative in both types of subjects. By way of comparison it may be remarked that the reaction following withdrawal of parathyroid extract is similar in patients with osteogenesis imperfecta and in normal persons.

In case 1 the magnesium balance, as shown in figure 5, became more markedly negative during the course of parathyroid medication owing to a rise in urinary and fecal magnesium, while in case 2 the magnesium balance remained essentially the same as during the control phase. In case 1 (periods 28 to 30) and case 2 (periods 32 to 34) there was a definite increase in the magnesium retention in the interval of rest following the withdrawal of parathyroid extract, this increase being due to a diminution in both the urinary and the fecal magnesium. In case 2 the response to parathyroid extract was less marked. It is barely possible that the viosterol (viosterol 10,000D) which had been given

TABLE 4.—*Comparison of the Effect of Parathyroid Extract on the Balances for Calcium and Phosphorus in Patients with Osteogenesis Imperfecta and in Normal Persons*

	Normal Persons (Albright et al.[65])	Patients with Osteogenesis Imperfecta
Urinary output	Calcium, increase Phosphorus, increase sometimes followed by a decrease	Calcium, increase Phosphorus, decrease followed by increase
Fecal output	Calcium, perhaps an increase Phosphorus, no change	Calcium, increase Phosphorus, usually increase
Total balance	Calcium, negative Phosphorus, negative	Calcium, negative Phosphorus, usually negative

two and one-half weeks previously had an influence on the action of the parathyroid extract in this case.

There was an increase in the urinary output and a drop in the fecal output of potassium with a slightly negative balance when parathyroid extract was administered, as shown for case 1 in figure 5. During the interval of rest there was a decidedly positive balance due to a marked decrease in the urinary and fecal potassium. In case 2 there was also a decrease in the potassium balance followed by an increase during the interval of rest. There was a slight decrease in the urinary sodium during the time the parathyroid extract was being given, but the total balance remained about the same. In both cases a marked decrease in the urinary sodium appeared immediately after the administration of parathyroid extract was discontinued, and the positive balance became more marked than it had been during the previous phase of the study. There was no change in the chlorine balance during the time in which parathyroid extract was administered, but after this there was a markedly positive balance, as shown for case 1 in period 28 (fig. 5),

which corresponded with the increased balance of sodium and potassium. In case 2 the effect was not so marked. The sulphur balance was diminished in both instances owing to a decrease in the urinary sulphur, and this decrease was followed by a definite increase in the balance during the interval of rest. There was no decided change in the nitrogen balance. However, in both instances there was an increase in

TABLE 5.—*Comparison of the Effects of Administration of Parathyroid Extract and Large Doses of Viosterol on the Balances for Magnesium, Potassium, Sodium, Chlorine, Sulphur and Nitrogen in Patients with Osteogenesis Imperfecta*

	Parathyroid Extract, 20 Units Daily	Viosterol 10,000 D From 0.1 to 0.5 Cc. Daily
Magnesium	Urinary, increase Fecal, no change Balance, negative balance increased After withdrawal, rapid recovery	Urinary, no change Fecal, slight increase Balance, negative balance slightly increased After withdrawal, slow recovery
Potassium	Urinary, decrease Fecal, increase Balance, decreased even to negative After withdrawal, marked retention	Urinary, possible slight increase Fecal, no change Balance, showing tendency to be negative After withdrawal, decrease in urinary output
Sodium	Urinary, increase Fecal, no change Balance, not affected After withdrawal, marked retention	Urinary, increase Fecal, no change Balance, negative After withdrawal, decrease in urinary output
Chlorine	Urinary, no change Fecal, no change Balance, not affected After withdrawal, marked decrease in urinary output with marked positive balance	Urinary, no change Fecal, no change Balance, not affected After withdrawal, decrease in urinary output with marked positive retention
Sulphur	Urinary, slight decrease Fecal, no change Balance, slightly increased After withdrawal, decrease in urinary output with retention	Urinary, slight decrease Fecal, no change Balance, showing slight retention After withdrawal, decrease in urinary output with retention
Nitrogen	Urinary, decrease Fecal, no change Balance, slightly increased After withdrawal, increase in retention	Urinary, decrease Fecal, no change Balance, slightly increased After withdrawal, increase in retention

the nitrogen retention during the interval of rest; this was due to a decrease in the urinary nitrogen. The effects produced by parathyroid extract on the mineral balances other than those of calcium and phosphorus are summarized in table 5 and compared with the changes produced in the balance for these elements by large doses of viosterol.

Influence of Viosterol and Parathyroid Extract on the Plasma Phosphatase.—The values for the activity of plasma phosphatase when determined under ordinary conditions, were well within the normal range. However, administration of parathyroid extract and of large

doses of viosterol caused a definite diminution in the activity of the enzyme. In both cases, as seen in table 6, a gradual decrease in the phosphatase coincided with increases in the dosage of viosterol. The same effect on the plasma phosphatase was observed in two other typical cases of osteogenesis imperfecta not described in this paper. Taylor, Weld, Banion and Kay [49] observed a similar lowering of the activity of plasma phosphatase in normal dogs when the animals were given parathyroid extract and large doses of viosterol.

Roentgenograms and Clinical Reaction During the Time of Study.—Roentgenograms made at frequent intervals showed no evidence of increased or decreased density of bone. No fractures occurred during the course of the study. There were no significant changes in the hemoglobin content, in the number of red and white cells or in the results of the

TABLE 6.—*Effect of Administration of Viosterol and Parathyroid Extract on the Activity of Plasma Phosphatase* *

	Date	Control Period	Viosterol	Parathyroid Extract
Case 1 (A. O.)	3/19/31	0.1270	.....	.....
	3/28/31	.....	0.1014	.....
	4/ 6/31	.....	0.0715	.....
	4/21/31†	.....	0.0544	.....
	5/ 9/31	0.1002	.....	.....
	5/18/31‡	.....	.....	0.0801
	5/30/31	0.0975	.....	.....
	6/14/31§	.....	0.0681	.....
	6/26/31	0.0955	.....	.....
Case 2 (D. J.)	3/19/31	0.1261	.....	.....
	3/28/31	.....	0.1030	.....
	4/21/31†	.....	0.0698	.....
	5/ 9/31	0.1041	.....	.....

* The values are expressed in units as defined by Kay.[59]
† After thirty-three day treatment with viosterol 10,000D, 0.1 cc., increasing to 0.5 cc. daily.
‡ After daily administration of parathyroid extract 20 units for nine days.
§ After daily administration of viosterol 10,000D, 0.5 cc. for fifteen days.

differential count and routine examination of the urine. No symptoms developed in case 1 after 0.5 cc. of 10,000D viosterol had been administered for fifteen days. In both patients slight anorexia and nausea developed after the thirty-three day course of viosterol therapy. D. J. (case 2) refused part of her food during the administration of parathyroid extract, and a slight fever developed. A. O. (case 1), however, was not outwardly disturbed in any way by the parathyroid extract.

COMMENT

The foregoing data confirm the view that one of the characteristic abnormalities in osteogenesis imperfecta is a deficiency in the retention of calcium and phosphorus under conditions which favor retention in normal persons. The evidence regarding a similar deficiency in mag-

nesium metabolism is suggestive but not conclusive. Whether or not this fault in metabolism is due to a lowered threshold for excretion of these elements or to a primary inability of the osseous tissues of the body to deposit and hold them in normal amounts cannot be determined from evidence now available. Except for this tendency to excrete an abnormally large proportion of the calcium and phosphorus ingested no evidence of hyperfunction of the parathyroid glands has been obtained. The finding of normal values for these elements in the blood and of essentially normal parathyroid bodies in the one patient who was examined at autopsy suggests at least that this cannot be the chief etiologic factor. The clinical picture, including the changes in the bones shown by roentgen examination, is not that commonly seen in patients with acquired hyperparathyroidism. The deficiency in the phosphatase activity of the periosteal and subperiosteal tissue, as described in a foregoing paragraph, appears to offer a more satisfactory lead for future investigation.

The responses of patients with osteogenesis imperfecta to parathyroid extract and to viosterol in various dosages are apparently not significantly different from those of normal persons. The fact that these agents only aggravate the existing abnormal tendency proves with certainty that hypoparathyroidism is not a feature of the pathogenesis and that the deficiency is in no way similar to that occurring in patients with rickets.

The data regarding the protein metabolism and all the features of the mineral exchanges of the body other than those mentioned indicate that the defect in metabolism in patients with osteogenesis imperfecta is confined fairly strictly to the mechanism of osseous growth and development.

SUMMARY AND CONCLUSIONS

The mineral balances were determined in two patients with typical osteogenesis imperfecta on a standard regimen known to favor growth and development in normal persons.

The effects on the mineral metabolism of feeding enormous doses of viosterol and of administering parathyroid extract subcutaneously were studies in the same two patients.

Under standard conditions (control period) both patients exhibited a deficiency in the retention of calcium, phosphorus and magnesium. No abnormality was discovered in reference to other features of the mineral metabolism during this period.

The most significant response to large doses of viosterol was the induction of a negative balance for most of the minerals, notably for calcium and phosphorus. The metabolism of nitrogen and sulphur underwent little, if any, change. The urinary output of calcium and phosphorus tended to increase, while the fecal output of these elements

was decreased. The influence of the viosterol persisted for several days after the medication was discontinued.

Parathyroid extract likewise caused an excessive output of calcium, phosphorus, magnesium, potassium and sodium. Its immediate effect was more marked than that of viosterol. The urinary tract was again the chief pathway for the increased excretion, the absolute losses by way of the intestinal tract increasing but slightly. Unlike viosterol, parathyroid extract had no sustained influence on the mineral exchange. A definitely positive balance for the chief elements was promptly reestablished after withdrawal of the hormone.

Comparison of the responses of the patients with osteogenesis imperfecta with those of normal persons revealed certain differences, the significance of which is not apparent.

The phosphatase activity of the blood plasma was found to be normal during the control phase of the study but was definitely diminished after the administration of parathyroid extract and of massive doses of viosterol.

Roentgen examinations of the bones made periodically showed no definite change during the course of the study.

While it cannot be concluded from the data thus far obtained that hyperfunction of the parathyroid glands is a factor in the pathogenesis of osteogenesis imperfecta, it is obvious that an extract of these organs (or large doses of the similarly acting viosterol) only accentuates the disturbance already present and therefore should not be employed therapeutically.

Case Reports

DUODENITIS IN CHILDHOOD

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Judd [1] in 1921 differentiated between duodenal ulcer and another duodenal lesion he proposed to designate as duodenitis. The true ulcer is characterized by a definite crater, an indurated border which is palpable and hyperemia and stippling of the peritoneal coat. The second variety produces hyperemia and stippling of the serosa, but the wall is not indurated and on palpation the duodenum is indistinguishable from one that is normal. On examination of the mucosa diffuse or local inflammation and at times one or more simple erosions may be found. McCarty [2] in 1924 found microscopic cellular destruction, congestion and edema with migration of leukocytes, lymphocytes and endothelial leukocytes. Konjetzny [3] concluded that duodenitis is an antecedent of duodenal ulcer since in a series of twenty-two cases of duodenal ulcers he found associated gastritis or duodenitis. This view has been opposed by others. Wellbrock [4] from histopathologic studies concluded that there is a relationship between duodenal ulcer and duodenitis, his conclusions being based on a similarity of changes in the ulcer and duodenitis. The effect of duodenitis on the development of ulcer requires further study.

Kirklin [5] in 1929 reported forty-five cases of duodenitis found at operation in which the diagnosis had not been made either clinically or roentgenographically. In his review of the roentgenologic data following surgical diagnosis he propounded several tentative criteria for the

1. Judd, E. S.: Pathologic Conditions of the Duodenum, Journal-Lancet **41**:215, 1921.

2. McCarty, W. C.: Excised Duodenal Ulcers: A Report of Four Hundred and Twenty-Five Specimens, J. A. M. A. **83**:1894 (Dec. 13) 1924.

3. Konjetzny, G. E.: Zur Pathologie und chirurgischen Behandlung des Ulcers duodeni, Deutsche Ztschr. f. Chir. **184**:85, 1924.

4. Wellbrock, W. L. A.: Duodenitis and Duodenal Ulcer, Ann. Surg. **91**: 533, 1930.

5. Kirklin, B. R.: A Roentgenologic Consideration of Duodenitis, Radiology **12**:377, 1929.

roentgenologic diagnosis of duodenitis: irritability of the bulb as shown by rapid emptying and pronounced but unstable deformity; indistinctness of the contour of the bulb; absence of a marginal niche or central fleck indicative of a crater, and absence or rarity of gastric retention. In 1934 [6] in an analysis of thirty-two cases of simple duodenitis in which ulcer and scars were definitely excluded, Kirklin's roentgenologic criteria were essentially those found in his previous study. First in importance was abnormally increased irritability of the duodenum, and, second, a mucosal pattern which was coarsely and irregularly reticular and appeared as clear islands lying in a denser network. The absence of an ulcer crater and complete absence of retention in uncomplicated duodenitis were the other essential points. Kirklin found the stomach small and hypertonic with active, and at times disordered, peristalsis.

Clinically, hemorrhage has occurred not infrequently and with considerable severity in duodenitis. Nagel [7] concluded that the clinical picture is identical with that of duodenal ulcer. Rivers [8] found that when duodenitis is associated with ulcer the syndrome is characteristic of ulcer. A number of authors have concluded that there is apparently no clearcut differentiation between the symptoms of ulcer and those of duodenitis.

We are reporting in this paper a case of duodenitis occurring in a child. In the literature we have been unable to find a report of this condition in childhood. Kennedy [9] has expressed the opinion that duodenitis, ileitis and jejunitis are not uncommon in children but that probably cases of each have been overlooked. It is well known that adults with peptic ulcer not infrequently give a history of typical symptoms of ulcer which began during childhood. From our own experience we believe that these rarely diagnosed lesions of the stomach and duodenum would be more frequently found if the possibility of their occurrence were borne in mind. The symptoms presented by the patient reported here were essentially those of peptic ulcer, and a clinical diagnosis of ulcer had been made. The diagnosis of duodenitis was made roentgenologically, according to criteria of Kirklin. This lesion of duodenitis in a child was of particular interest to us because recently we have reported elsewhere [10] a case of duodenal ulcer occurring in a girl 4 years old. Our

6. Kirklin, B. R.: Duodenitis and Its Roentgenologic Characteristics, Am. J. Roentgenol. **31**:581 (May) 1934.

7. Nagel, G. W.: Duodenitis, in Collected Papers of the Mayo Clinic, Philadelphia, W. B. Saunders Company, 1926, vol. 18, p. 153.

8. Rivers, A. B.: A Clinical Study of Duodenitis, Gastritis, and Gastrojejunitis, Ann. Int. Med. **4**:1265, 1931.

9. Kennedy, R. L. J.: Personal communication to the authors.

10. Gillespie, J. B., and Gianturco, C.: Peptic Ulcer in Childhood, Illinois M. J. **67**:160 (Feb.) 1935.

observation of two instances of this supposedly rare lesion within a short time has suggested that a study of this condition in children deserves more attention.

REPORT OF A CASE

The patient, a girl, was 12 years old. The family history was essentially irrelevant. There was an older sister who was alive and well. The patient had had measles, chickenpox and pertussis. She had not begun to menstruate.

She was first seen on Aug. 27, 1934. She complained of abdominal discomfort of eight months' duration. In December 1933 she moved from Akron, Ohio, to Urbana. At that time both she and her sister began to complain occasionally of abdominal discomfort and lassitude for periods of about one day. The attacks

Spastic deformity of the duodenal bulb.

became less frequent, and the older sister ceased to have any difficulty in a short time. The patient returned to Akron for two months during the summer of 1934, and the attacks stopped. However, after returning home they began again. The mother thought it might be due to the change of drinking water. The abdominal pain was not acute, occurred only at night and awakened the patient from sleep. The discomfort was relieved by soda or magnesia magma. She did not know whether milk relieved the discomfort. She vomited once with the pain. There was no knowledge of whether relief was given by food or of whether there was a relationship to meals. The patient was chronically constipated. Her appetite was poor because she was afraid that food might cause the pain.

The patient was slender, healthy-looking and somewhat high-strung. Her weight was 77½ pounds (35.1 Kg.) and her height 59¼ inches (150.4 cm.). Normal weight for her age is 93 pounds (42.2 Kg.). The blood pressure was 115 systolic and 75 diastolic, the pulse rate was 88 and the temperature was 99.8 F. The tonsils were cryptic, infected and enlarged. The cervical glands were

enlarged. Otherwise physical examination gave essentially negative results. There were no abdominal tenderness and no masses. Rectal examination and urinalysis gave negative results. Examination of the blood revealed: hemoglobin, 88 per cent; erythrocytes, 5,250,000, and leukocytes, 10,000, of which 54.5 per cent were lymphocytes, 39 per cent neutrophils and 6.5 per cent eosinophils. The Wassermann reaction of the blood was negative. The Mantoux test with 0.1 mg. of old tuberculin was negative. Examination of the stool revealed no blood. Gastric analysis showed free hydrochloric acid, 16, and total acids, 32. Roentgenograms of the chest and colon gave negative results. The fluoroscopic and roentgenographic examination of the stomach and duodenum revealed duodenitis. The figure shows the bulbar deformity.

The girl was given milk and cream every hour, with alternating doses of a preparation containing bismuth subnitrate, magnesium carbonate and sodium bicarbonate and tablets containing calcium carbonate and magnesium oxide every hour. Small doses of tincture of belladonna were administered. After five days the patient was given a bland diet. This was continued for one week, after which the milk and cream between feedings were discontinued and a more inclusive bland diet was allowed. Since treatment was instituted there has been no abdominal discomfort, and her appetite has improved remarkably. She has gained weight consistently.

COMMENT

From a study of this case we were not impressed by any symptoms which might be characteristic of the duodenitis syndrome. Kirklin has shown roentgenographically that duodenal ulcer and diffuse duodenitis may occur together; this has been verified surgically. The symptoms generally were those leading clinically to a diagnosis of peptic ulcer. Pain and constipation were the cardinal complaints. The observation of recurring gastric discomfort and constipation in a slender child suggests peptic ulcer or duodenitis. A complaint of abdominal pain, particularly occurring at night and relieved by the ingestion of soda, should be an indication for roentgen examination of the stomach and duodenum by a competent roentgenologist. The history, however, is rarely typical, and roentgen studies of the stomach and duodenum are justified in cases of obscure gastric discomfort.

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HYPOGLYCEMIA IN THE NEW-BORN

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There is considerable literature on the subject of hypoglycemia in adults, both with and without insulin therapy. Very little, however, has been written concerning the state of hypoglycemia as a cause of symptoms in new-born infants. The effect of hypoglycemia in the production of neurologic symptoms in adults has been well described by Banting and his coworkers.[1]

Britton [2] noted that the blood sugar of new-born kittens was usually maintained at a normal level even though the mother's blood sugar was severely reduced by insulin or greatly increased by epinephrine or dextrose. Bowen and Heilbrun,[3] however, reported instances in which the fetus of a diabetic mother had hypertrophic islands of Langerhans in the pancreas.

In the literature on diabetes during pregnancy very little is said concerning the sugar metabolism of the child after birth. Stander and Peckham [4] have expressed the opinion that the excessive size of many of the babies of diabetic mothers is probably due to the increased amount of sugar in the maternal blood, thereby making it easier for the fetus to obtain a liberal supply of carbohydrate. It is believed that insulin exerts no deleterious effect on the baby but that insufficient treatment of the mother may result in an extra strain on the pancreas of the fetus and produce an excessive development of the islet tissues. This has been mentioned as a possible cause of hypoglycemia after birth. Gray and Feemster [5] reported a case in which the child of a diabetic mother had hypoglycemia, with a blood sugar value of 0.067 per cent on the third day of life. The child died on the fourth day, and the

1. Banting, F. G.; Campbell, W. A., and Fletcher, A. A.: Further Clinical Experience with Insulin in the Treatment of Diabetes Mellitus, Brit. M. J. **1**:8 (Jan. 6) 1923.

2. Britton, S. W.: Maternal and Fetal Blood Sugar Changes Under Various Experimental Conditions, Am. J. Physiol. **95**:178, 1930.

3. Bowen, B. D., and Heilbrun, N.: Pregnancy and Diabetes, Am. J. M. Sc. **183**:803, 1932.

4. Stander, H. J., and Peckham, C. H.: Pregnancy and Diabetes, Am. J. Obst. & Gynec. **14**:313, 1927.

5. Gray, S. H., and Feemster, L. C.: Compensatory Hypertrophy and Hyperplasia of the Islands of Langerhans in the Pancreas of a Child Born of a Diabetic Mother, Arch. Path. **1**:348 (March) 1926.

pancreas showed an increase of the island tissue to twenty-four times the normal amount.

I have not found any reference to a state of hypoglycemia producing symptoms in the new-born offspring of a nondiabetic mother. It occurred to me that the two following cases might be of interest because of the striking similarity of the symptoms and findings, although one child was born of a diabetic mother and the other of a woman with normal sugar metabolism.

REPORT OF CASES

CASE 1.—*History.*—R. S. was born on Aug. 21, 1931, at United Hospital. Birth was normal. The mother, aged 30, American-born of Italian extraction, had always been well up to 1925 except for "kidney trouble" during the first pregnancy ten years before the present admission. The child of that pregnancy was living and well. Two subsequent pregnancies resulted in one premature child which lived only a few hours and one full term stillbirth. The mother stated that all the babies were very large at birth. In 1925 the mother was discovered to be diabetic. She had been under rather haphazard treatment since, with a regulation of diet and 25 units of insulin daily. She had always been careless about her diet and use of insulin but had never been in a coma.

The present pregnancy was uncomplicated except for some edema of the legs. She had taken insulin more or less regularly and took 25 units on the morning of August 20. That day the attending doctor decided to induce labor because of the large size of the fetus. He ordered castor oil and quinine which resulted in the onset of labor that night. The estimated term was eight and a half months.

The mother was admitted to the hospital in active labor the morning of August 21 and was delivered spontaneously of a living male child weighing 9 pounds and 14 ounces (4,195.73 Gm.). The child breathed promptly and appeared to be normal in every respect for the first twenty-four hours. He went to the breast at the end of the first twelve hours and nursed well. Sweetened water was supposed to be offered between feedings, but it was not stated in the nurse's notes whether he took any appreciable amount.

After the 10 a. m. feeding on August 22 the nurse noticed evidence of nervous irritability. A few minutes later the child became cyanotic and had a fine tremor of the arms and legs. This was followed shortly by a clonic convulsive seizure involving the right arm and leg. The convulsions recurred about every thirty minutes at first and then became more frequent and more severe. Between attacks the child seemed very drowsy and pale.

When I saw the child about 11 a. m. he was semicomatose and pale, with clammy skin. He was having frequent convulsive seizures of the clonic type. These convulsions resembled those seen in infants with birth injury, but the child's condition appeared different between attacks. There was no rigidity of the neck or extremities, the fontanel was flat and it was difficult to elicit the reflexes. The general physical examination was not of interest.

Because of the history of diabetes in the mother, blood was immediately obtained by puncture of the longitudinal sinus. Examination revealed: sugar, 47 mg. per hundred cubic centimeters; urea nitrogen, 10.2 mg., and the Wassermann reaction, negative. Spinal puncture yielded a clear fluid which was reported normal by the laboratory. A roentgenogram of the mediastinal region showed no evidence of thymic enlargement.

Treatment.—The child was given 20 cc. of whole blood from the mother (whose blood sugar at this time was 374 mg. per hundred cubic centimeters) intramuscularly and 100 cc. of 5 per cent dextrose solution subcutaneously at once. He was fed 3 ounces (148.8 cc.) of a 1:8 solution of condensed milk by gavage every four hours and was offered 10 per cent dextrose solution by mouth between feedings.

Course.—The convulsive seizures became less frequent within a few hours and had ceased entirely by 10 p. m. Another hypodermoclysis of 100 cc. of 5 per cent dextrose solution was given. There were no further attacks during the night, and the child took the bottle well.

At 10 a. m. on August 23 the blood sugar was 68 mg. per hundred cubic centimeters, and the child appeared normal on examination. He was given a second injection of the mother's blood and a formula of lactic acid, evaporated milk and karo. He took his feedings well and began to gain weight.

On August 26 the blood sugar was 75 mg., and the child was progressing normally. He was discharged on August 31 in good condition.

The subsequent course up to the age of 3 years has been perfectly normal as regards the carbohydrate metabolism, in spite of a prolonged siege of pneumonia and empyema at the age of 3 months.

CASE 2.—*History.*—H. F., a boy, was born on Sept. 21, 1933, of American parents. The family history had no evidence of any metabolic disease. The mother had been well before and throughout this, her first pregnancy.

The child was born spontaneously and was apparently normal for the first twenty-four hours after birth. After the morning nursing on September 22 the nurse noted signs of increasing nervous irritability. About 10 a. m. the child refused to nurse and shortly after that had a convulsive seizure of the clonic type. He was very drowsy after the seizure. The convulsions were repeated frequently, especially if the child was handled.

The patient was seen by me at noon. He was pale, the skin was clammy, the fontanel was flat, there was no rigidity of the neck or extremities between attacks, and it was hard to elicit the reflexes. Otherwise the results of the general physical examination were irrelevant. The Moro reflex reaction was normally active.

Blood obtained from the longitudinal sinus showed: sugar, 50 mg. per hundred cubic centimeters, and calcium, 12.5 mg. Spinal puncture yielded fluid that was normal except for a few fresh red blood cells.

Treatment.—An intramuscular injection of 20 cc. of whole blood from the mother and a subcutaneous injection of 50 cc. of 5 per cent dextrose solution was administered at once. He was fed 3 ounces of 7 per cent dextrose and 3 per cent gelatin in physiologic solution of sodium chloride by gavage every four hours and was offered 10 per cent dextrose solution by mouth. One-fourth grain of phenobarbital sodium was put in the feeding every eight hours.

Course.—The convulsions ceased within two hours, and the nervous irritability gradually diminished until the child appeared to be normal at 10 p. m. On September 23, the child appeared to be perfectly normal and was taking the bottle well. He was then put on a routine formula of milk, sugar and water. A second determination of the blood sugar was not made because of the obvious normality of the child and the serious objection of the mother to further puncture of the fontanel. The child has been followed since and is now a normal boy 11½ months of age weighing 22½ pounds (10,200 Gm.).

COMMENT

Two cases have been reported which appear to me identical in every respect except in the family history. It is an open question whether the insulin taken by the mother of the patient in the first case had any effect in producing the hypoglycemia in her baby. Certainly there was no exogenous insulin in the second case.

It seems likely to me that some of the cases of convulsive attacks during the first few days of life which are now considered to result from birth injury may be due to hypoglycemia. I feel that a reading of the blood sugar should be made in all these cases before a diagnosis is made. It seems reasonable to suppose that without proper treatment one or both of my patients might have died owing to a continued fall of the blood sugar level. Babies take food with great difficulty after severe hypoglycemia develops, and without the use of gavage and parenteral administration of sugar the deficiency of sugar in the blood might not be corrected.

264 King Street.

INTERMITTENT AND CONTINUOUS RENAL GLYCOSURIA

REPORT OF THREE CASES

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The repeated appearance of dextrose in the urine of a child usually but not invariably indicates diabetes mellitus. Because diabetes mellitus is always a serious metabolic disorder in a child it is important to realize that recurring nondiabetic glycosuria can also occur in childhood. There are several types of nondiabetic or renal glycosuria, and it is my purpose in this paper to describe them as they occurred in 3 children who were thought at first to have diabetes mellitus.

REPORT OF CASES

CASE 1.—P. B., a boy aged 7 years, of Irish parentage, was admitted to the Mount Sinai Hospital for the first time on June 16, 1932. His mother was said to be diabetic. Her urine was examined on numerous occasions, but in spite of an unrestricted carbohydrate intake she did not always have glycosuria. She had never required treatment with insulin. The sugar content had not exceeded 0.5 per cent in any specimen which had been examined, and there was no acetonuria. She brought her child to the outpatient department because of failure to gain weight. Sugar and acetone were found in his urine. Since he weighed only 35 pounds (15.9 Kg.) at the age of 7 years the glycosuria together with the acetonuria strongly suggested the existence of diabetes mellitus. There was, however, no history of polyuria or polydipsia. The physical examination gave negative results except for the evident malnutrition. A visit to the child's home revealed a deplorable domestic situation; therefore, it was felt that the malnutrition from which he suffered was partially, if not entirely, due to underfeeding. He was admitted to the hospital for study. Analysis of several specimens of urine revealed 0.6 per cent of sugar and a trace of acetone; other specimens were entirely normal. The blood sugar after fasting was 50 mg. per hundred cubic centimeters. The child ate the regular ward diet ravenously for the first few days in the hospital. Coincidentally the acetonuria disappeared.

The concentration of blood sugar after the ingestion of 30 Gm. of dextrose showed a rise to 225 mg. per hundred cubic centimeters in one hour followed by a sharp drop to 70 mg. in two hours. When the blood sugar content of 175 mg. per hundred cubic centimeters was obtained after the first half hour glycosuria was already present, indicating that dextrose was passing into the urine before the blood sugar content had risen to that point.

In order to test the tolerance for carbohydrate, the child was given a daily diet of carbohydrate, 85 Gm., protein, 50 Gm. and fat, 95 Gm., with no insulin.

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There was no glycosuria. After a few weeks he left the hospital and was seen regularly in the clinic for patients with diabetes, where the specimens of urine at first gave negative results. The diet was increased gradually until he was receiving carbohydrate, 170 Gm., protein, 60 Gm. and fat, 100 Gm., with no insulin. With the increased intake of food, sugar was present occasionally in the urine, not exceeding 0.6 per cent in any specimen. During a year and a half he gained 9 pounds (4.1 Kg.).

On his second admission to the hospital, in January 1934, the child's general physical condition had improved markedly. Urinalysis revealed the occasional presence of sugar, which did not exceed 0.6 per cent, and a trace of acetone. The child's diet was increased until it contained 200 Gm. of carbohydrate daily. In

TABLE 1 (*Case* 1)—*Results of Sugar Tolerance Test During the First Period of Hospitalization* *

	Blood Sugar, Mg.	Urine Sugar, Percentage	Acetone
Fasting	60	0	
½ hour	175	0.7	
1 hour	225	4.5	0
1½ hours	175	5.5	0
2 hours	70	5.0	0
3 hours	65	0.4	0

* Thirty grams of dextrose was used.

TABLE 2 (*Case* 1).—*Results of Sugar Tolerance Test During the Second Period of Hospitalization* *

	Blood Sugar, Mg.	Urine Sugar, Percentage	Acetone
Fasting	70	0	0
½ hour	145	0	0
1 hour	155	1.0	0
2 hours	115	2.3	0
3 hours	110	4.0	0
5 hours	...	0.5	0
7 hours	...	0	0

* Thirty-five grams of dextrose was used.

spite of the increased intake the amount of sugar in the urine did not increase. A test for blood sugar taken two hours after a meal which contained 67 Gm. of mixed carbohydrate was 105 mg. per hundred cubic centimeters. The test for sugar tolerance was repeated, with the results shown in table 2.

The blood sugar did not rise as high as in the previous test (table 1). Sugar was present in the urine when the blood sugar concentration was 155 mg. per hundred cubic centimeters. Glycosuria, therefore, occurred before the blood sugar had reached that level.

The patient's tolerance for levulose and galactose was studied. Since there was only a slight elevation in the blood sugar, no glycosuria resulted. The test, therefore, did not demonstrate whether or not there was a diminished threshold for these substances. This would have been possible only if the blood sugar concentration had risen to an appreciable extent.

The differential diagnosis in this case lay between early diabetes mellitus and a type of renal glycosuria in which only occasional specimens contain sugar. At the time of the child's first admission to the hospital it was not possible to differentiate absolutely between the two conditions. The blood sugar curve (table 1) strongly suggested diabetes because of the rapid rise to 225 mg. The sugar content was as high as 5.5 per cent in a single specimen of urine. This likewise suggested diabetes. There was, on the other hand, a rapid fall in the blood sugar to 70 mg. two hours after the ingestion of dextrose. This usually does not occur in diabetes. Some writers [1] have stressed the occurrence of hyperglycemia as revealed in the test for sugar tolerance as indicative of latent diabetes. Apparently in this patient the height of the curve did not indicate a permanently damaged tolerance for carbohydrate, since the blood sugar fell to normal two hours after the ingestion of dextrose. The abnormal rise more likely was incident to "hunger diabetes," as suggested by the abnormally poor state of the child's nutrition and by the acetonuria which promptly disappeared with the administration of food. When the sugar tolerance was retested one year later a normal response was elicited (table 2), which definitely ruled out diabetes mellitus. Starvation and ketosis produce transient glycosuria due to a disturbed carbohydrate metabolism, and if the dextrose tolerance is tested in the ketotic state a diabetic type of blood sugar curve is obtained.[2] With the renal threshold lower than normal, any condition producing hyperglycemia will increase the glycosuria. In case 1 there were both hyperglycemia during the dextrose tolerance test and increased glycosuria when the patient's state of nutrition indicated that he was still "starving." One year later, however, there was a normoglycemic response, and the glycosuria was less intense. The child's state of nutrition in the meantime had improved markedly. He had gained 9 pounds in eighteen months on a relatively normal diet without the use of insulin, which, together with the fact that the urine was usually sugar-free during that period of observation, strongly suggested the presence of nondiabetic glycosuria. When sugar was excreted the amount did not exceed 0.6 per cent in any specimen. Acetonuria was not present. The excretion of small amounts of sugar is not usual

1. Sherrill, J. W.: The Diagnosis of Latent and Incipient Diabetes, J. A. M. A. **77**:1779 (Dec. 3) 1921. John, H. J.: A Summary of Findings in One Thousand One Hundred Glucose Tolerance Estimations, Endocrinology **13**:388 (Aug.) 1929. Joslin, E. P., and Pincus, G.: The Inheritance of Diabetes, J. A. M. A. **103**:105 (July 14) 1934.

2. Kohn, J. L.; Fries, M. E., and Felshin, G.: Spontaneous and Induced Ketosis in Children: Effect on the Glucose Tolerance Test, Am. J. Dis. Child. **34**:857 (Nov.) 1927.

in a diabetic child who is receiving a relatively normal diet (carbohydrate, 170 Gm., protein, 60 Gm., and fat, 100 Gm.) with no insulin.

It was therefore concluded that the patient had a type of renal glycosuria in which dextrose was present in the urine only when the concentration of blood sugar exceeded a rather high level. For this reason the glycosuria was intermittent. The sugar tolerance test (table 2) showed conclusively that the urine was sugar-free as long as the blood sugar content remained below 145 mg. The exact point at which sugar first began to appear in the urine was probably somewhat below that figure. However, on the regimen which permitted 67 Gm. of carbohydrate at each meal there was only occasional glycosuria, because the rate of absorption of carbohydrate following a regular meal was slow enough to prevent the blood sugar from exceeding the renal threshold. The normal gain in weight, together with growth and body development, indicated also that the child had glycosuria of nondiabetic origin. The usual course in the early stages of diabetes is one of

TABLE 3 (*Case 2*).—*Results of Sugar Tolerance Test* *

	Blood Sugar, Mg.	Urine Sugar, Percentage	Acetone
Fasting	90	0	0
½ hour	125	0	0
1 hour	135	0.6	0
1½ hours	125	0.8	0
2½ hours	110	0.4	0

* Seventy-five grams of dextrose was used.

stationary weight followed by increased glycosuria when the requirement of food is increased in order to secure proper growth. Nor has it been possible in a series of sixty-three diabetic children under observation at the present time to obtain an appreciable gain in weight over a period of eighteen months without the aid of insulin.

The patient was in good physical condition when seen in May 1934, twenty-three months after his first admission to the hospital. A casual specimen of the urine at that time contained 0.4 per cent of sugar. There was no acetonuria. There had been a further gain in weight.

CASE 2.[3]—J. Z., a Jewish boy aged 13 years, an only child, was seen for the first time in 1931. There was no history of diabetes in the family. The urine of both parents was normal. Sugar had been noted frequently in the patient's urine during the past three years, but in spite of this he had grown normally. He excreted about 10 Gm. daily. Diabetes mellitus was suspected, and a sugar tolerance test was made (table 3).

In 1932 the patient excreted from 12 to 15 Gm. of sugar daily. The blood sugar content after fasting was again 90 mg. per hundred cubic centimeters.

3. This case is reported through the courtesy of Dr. Leo Mishkin.

There was no polyuria or nocturia. He had gained weight and therefore had purposely avoided an excessive intake of carbohydrate. The blood sugar content after fasting in 1933 was 90 mg. Because the early morning specimen was sugar-free it was decided to test his urinary output accurately over a period of days. It was found that the urine was usually entirely sugar-free in the early morning and that the glycosuria increased slightly during the day, reaching its height in the evening. The output remained fairly constant, ranging from 12 to 15 Gm. daily.

This patient had a type of renal glycosuria in which sugar appeared in the urine when the blood sugar content was above 90 and below 135 mg., for when that point was reached in the dextrose tolerance test the patient had well marked glycosuria. No diabetic symptoms occurred. The fact that this patient had been observed for six years without showing clinical symptoms of diabetes ruled out that diagnosis. The glycosuria occurred in the blood sugar at a somewhat lower level than in case 1. For this reason glycosuria was noted daily. The

TABLE 4 (*Case 3*).—*Results of Sugar Tolerance Test* *

	Blood Sugar, Mg.	Urine Sugar, Percentage	Acetone
Fasting	110	3.3	0
½ hour	190	2.6	0
1 hour	170	3.3	0
2 hours	145	4.0	0
3 hours	115	2.6	0

* Twenty-five grams of dextrose was used.

urine was sugar-free only when the patient was in the fasting state or when the blood sugar content approximated 90 mg. or less.

CASE 3.—V. N., a girl aged 2 years and 7 months, of Italian parentage, was admitted to the hospital on Nov. 24, 1933, with a diagnosis of diabetes mellitus. A reducing substance had been found in the urine when the child was 15 months of age. The family history was interesting in that a sister was said to have had diabetes for the past four years. The child's grandfather had supposedly died of diabetes.

The child's weight was 30 pounds (13.6 Kg.), which was normal for her age. Physical examination gave negative results. The blood sugar after fasting was 80 mg. per hundred cubic centimeters. The amount of sugar in the urine varied from 1 to 5 per cent, and averaged 10 Gm. daily. There was no acetonuria. Every specimen of urine contained sugar. Since continuous glycosuria occurred with a normal blood sugar value, a provisional diagnosis of renal glycosuria was made. Furthermore, in spite of the presence of glycosuria for at least sixteen months, the child had gained weight without restrictions of diet or the use of insulin. The dextrose tolerance curve (table 4) showed a normal response and confirmed the diagnosis of renal glycosuria.

Attempts were made to influence the output of sugar in various ways. When the child was placed on a diet low in carbohydrate the output of sugar fell to 4 Gm. daily. On a diet high in carbohydrate as much as 19 Gm. daily was excreted.

Diet, therefore, was a factor in this child's glycosuria, the excretion being greater when hyperglycemia occurred.

The effect of insulin was then studied. The patient was given 10 units of insulin after fasting for twelve hours. The blood sugar dropped to 60 mg. per hundred cubic centimeters. The glycuresis, however, continued, indicating a very low renal threshold.

As the child was continually excreting sugar, an attempt was made to demonstrate how readily acetonuria developed. This was tested by gradually reducing the amount of carbohydrate in the diet. Acetonuria appeared when the daily intake of carbohydrate was still as high as 55 Gm. daily, the total diet containing: carbohydrate, 55 Gm., protein, 45 Gm. and fat, 75 Gm.

A test for xylose tolerance was made in order to test the excretory ability of the kidneys for that substance. The child's output was 5.31 Gm. in twenty-four hours, which was slightly greater than normal. A test for galactose tolerance showed a low normal excretion of 1.3 Gm. in twenty-four hours. The elimination of phenolsulphonphthalein was 75 per cent in two hours. The blood urea was 9 mg. per hundred cubic centimeters, the blood calcium, 10.5 mg., and the blood cholesterol, 310 mg. of which 155 mg. was ester.

Theobromine salicylate was given in order to determine whether glycosuria could be increased by means of this drug. While there was no increase in the actual amount of sugar eliminated there was moderate diuresis. The urinary output increased from a daily average of 350 cc. to 550 cc. while the drug was being taken.

This child excreted sugar continually because of a very low renal threshold for that substance. Not one of several hundred specimens of urine was free from sugar. The glycosuria in this case was first noted at the age of 15 months. Except for the patient of Landabure,[4] this patient is the youngest whose case is recorded in the literature.

Two other instances of renal glycosuria were encountered in the family. A sister, aged 20 years, had had glycosuria for at least four years. Although she had no symptoms of diabetes she had been refused employment because of "diabetes" when she was 16 years of age. The blood sugar after fasting was 88 mg. Every one of many specimens contained sugar, the amount averaging 2 per cent. Acetonuria was occasionally present. The relation of the glycosuria to the intake of carbohydrate was studied with the result that the glycosuria definitely decreased when the patient was given a diet low in carbohydrate.

Specimens of the urine of twenty-two close relatives were also examined. One other instance of glycosuria was discovered. S. N., 22 years old, the patient's brother, had marked glycosuria and acetonuria, 2.8 and 6.6 per cent of sugar being present in morning specimens obtained on different days. In spite of the large amount of sugar excreted, there were no symptoms of diabetes, and he was totally unaware previously of the presence of glycosuria. His blood sugar after fasting was 95 mg.

4. Landabure, P. B.: Glucosuria infantil nondiabética, Semana méd. **37**:1358 (Oct. 30) 1930.

COMMENT

Three instances of nondiabetic glycosuria in children have been described. Each patient was studied for a sufficient length of time to confirm the diagnosis of benign glycosuria. The observations in these 3 cases offer a basis for reconsidering the subject of renal glycosuria.

Holst,[5] Fanconi,[6] Marble[7] and others who have written on renal glycosuria have separated what they call true renal glycosuria from other types of benign glycosuria. They have laid down certain criteria as essential for the diagnosis of renal glycosuria, namely: The substance found in the urine must be dextrose; the symptomatology of diabetes mellitus must be absent; a sufficient length of time must elapse before one can assume the presence of benign glycosuria, and the blood sugar tolerance curve must be normal. The occurrence of benign glycosuria in a relative is also emphasized. In addition, recently Marble stressed the point that every specimen of urine must contain sugar. This rigid rule would therefore exclude from the group known as cases of renal glycosuria all those in which dextrose is observed in the urine intermittently. According to the strict interpretation of this classification, therefore, only case 3 of this report would be considered as an example of renal glycosuria. It is obvious, however, that the presence of glycosuria in each of the three cases was dependent solely on the height of the renal threshold. In case 1 glycosuria appeared when the amount of sugar in the blood exceeded approximately 135 mg., and in case 2, when a value somewhere between 90 and 135 mg. was reached, whereas in case 3 the renal threshold was so low that glycosuria was continuous. The clinical course in the first 2 cases was just as benign as in case 3. The dextrose tolerance curves in all three cases were normal. The mother of the patient in case 1 had sugar in her urine on some examinations. Like her son she had intermittent glycosuria. On the other hand, 3 persons in the family of the patient in case 3 who had glycosuria all had a very low renal threshold. Studies on the sister, E. N., showed glycosuria when the blood sugar after fasting was 88 mg. The brother had 6 per cent of sugar in an early morning specimen and a blood sugar content of 95 mg. after fasting.

Therefore, in 2 of the 3 cases of benign glycosuria which have been described there was a similar type of glycosuria in members of the family, continuous in three members of one family and intermittent in

5. Holst, J. E.: Investigations into Benign Glycosuria and Diabetes Mellitus, Acta med. Scandinav. **63**:47, 1925.

6. Fanconi, G.: Die nicht diabetischen Glykosurien und Hyperglykämien des älteren Kindes, Jahrb. f. Kinderh. **133**:257 (Nov.) 1931.

7. Marble, A.: Renal Glycosuria, Am. J. M. Sc. **183**:811 (June) 1932.

two members of the other. These differences were due solely to the height of the threshold. It would seem that not only is the lowered threshold familial but even its degree. Bowcock [8] and Holst,[9] however, have reported that diabetes and renal glycosuria can occur in the same family. Marble, for example, found that in 11 of 15 cases of renal glycosuria (with a low threshold) there was a history of glycosuria in a member of the family. White,[10] in referring to what she has termed the "unclassified glycosurias," stated that glycosuria was present in a member of the family in 40 per cent of the cases of that type studied in the Joslin Clinic. She separated patients with "unclassified glycosuria" from those with renal glycosuria, using the latter definition only for the condition of those who had glycosuria continually. Joslin and White [11] in 1929 reported on 114 children with known glycosuria who had been examined since 1896. In this group were 8 patients who had what the authors termed true (low threshold) renal glycosuria. Of the 84 patients with "unclassified glycosuria" only 1 had become truly diabetic, 1 died and 4 were untraced. In 106, or possibly 110, of the 114 children diabetes had not developed despite former glycosuria. Both the type hitherto called "renal glycosuria" and that known as "unclassified glycosuria" have a striking familial incidence, indicating hereditary relationship. Joslin and White's careful reexamination of the patients with "unclassified glycosuria" has confirmed the benign nature of the condition. To exclude these patients from the group with renal glycosuria and to place them in a separate category serves to confuse the identity of the condition.

Little is known of the pathologic physiology of the kidney in cases of renal glycosuria, and therefore explanations of its existence are based on theoretical considerations. The modern conception of urinary secretion is based on the experiments of Wearn and Richards,[12] who demonstrated that sugar is excreted by the glomerulus and is reabsorbed in the renal tubules. While ordinarily sugar passes into the urine at approximately the same level, in certain conditions, notably during preg-

8. Bowcock, H. M.: Familial Glycosuria: Report of a Large Family, Ann. Int. Med. **2**:923 (March) 1929.

9. Holst, J. E.: The Occurrence of Benign Glycosuria in Diabetic Families, Arch. Int. Med. **38**:279 (Sept.) 1926.

10. White, P.: Diabetes in Childhood and Adolescence, Philadelphia, Lea & Febiger, 1932, p. 67.

11. Joslin, E. P., and White, P.: Diabetic Children, J. A. M. A. **92**:143 (Jan. 12) 1929.

12. Wearn, J. T., and Richards, A. N.: Observations on the Composition of Glomerular Urine, with Particular Reference to the Problem of Reabsorption in the Renal Tubules, Am. J. Physiol. **71**:209 (Dec.) 1924.

nancy, sugar is more readily excreted. This was well illustrated in the reports of Faber [13] and Bowcock and Greene.[14] They reported the cases of several patients with renal glycosuria who during pregnancy excreted more sugar than previously. In the postpartum period, on the other hand, there was a marked decrease in the excretion of sugar, probably caused by the fact that more carbohydrate was required for the formation of lactose by the mammary glands and therefore less was present in the blood passing through the kidney. In cases of renal glycosuria one must assume that there is some pathologic change in the function of the renal tissues which either enhances the excretion of sugar or prevents its reabsorption. The extent of the involvement probably explains the continued output of sugar in some cases and the intermittent output in others.

The occasional appearance of glycosuria incident to a cerebral lesion or trauma must, of course, be borne in mind.[15] One can hardly consider an alteration in the brain as the primary cause of renal glycosuria in the long-standing cases, for the familial nature of the disease would exclude that conception in most instances. Nor are conclusions justified from the unsubstantiated experiments of Goldberg,[16] who attempted to place the cause of renal glycosuria in the vegetative nervous system. It has been demonstrated by Powelson and Wilder,[17] Constam,[18] Allan and Vanzant,[19] Fanconi [6] and Shafton and Poncher [20] that the injection of insulin and the subsequent reduction of blood sugar do not eliminate glycosuria. In Allan and Vanzant's [19] case sugar was still being excreted when the blood sugar had fallen to 44 mg. In view of the low threshold in case 3 insulin was given in order to determine how low the blood sugar would fall before the urine was free from sugar. As anticipated, insulin failed to prevent glycosuria, even though the blood sugar dropped to 60 mg. Glycosuria, however, was decreased over a period of time

13. Faber, K.: Benign Glycosuria Due to Disturbances in the Blood Sugar Regulating Mechanism, J. Clin. Investigation **3**:203, 1927.

14. Bowcock, H. M., and Greene, E. H.: Observations in a Case of Renal Glycosuria During and After Pregnancy, J. A. M. A. **90**:502 (Feb. 18) 1928.

15. Allen, F. M.; Wishart, M. B., and Smith, L. M.: Three Cases of Renal Glycosuria, Arch. Int. Med. **24**:523 (Nov.) 1929.

16. Goldberg, M.: Der Einfluss des vegetativen Nervensystems auf die renale Glykosurie, Ztschr. f. d. ges. exper. Med. **59**:468, 1928.

17. Powelson, H. C., and Wilder, R. M.: Innocent Glycosuria, J. A. M. A. **96**:1562 (May 9) 1931.

18. Constam, G. R.: Ueber renale Glykosurie, Ztschr. f. klin. Med. **113**:281 (May 23) 1930.

19. Allan, F. N., and Vanzant, F. R.: Renal Glycosuria with Ketosis During Surgical Complications, Am. J. M. Sc. **180**:670 (Nov.) 1930.

20. Shafton, A. L., and Poncher, H. G.: Renal Glycosuria in Childhood, Am. J. Dis. Child. **47**:1323 (June) 1934.

by the administration of a diet low in carbohydrate. During a seven day test period the average daily excretion of sugar was 4.4 Gm. when a diet of carbohydrate, 60 Gm., protein, 60 Gm., and fat, 100 Gm., was ingested. When the diet was increased to carbohydrate, 150 Gm., protein, 60 Gm., and fat, 90 Gm., the daily output of sugar rose to an average of 11.2 Gm. Shafton and Poncher showed that glycosuria increases slightly with an increased intake of carbohydrate, and their table (C) demonstrated that the maximum output of sugar was greater when a more liberal intake of carbohydrate was offered. Fanconi and Constam made similar observations. In case 3 the excretion of sugar varied throughout the day but was usually highest in the early evening. This was undoubtedly due to a normoglycemic rise in blood sugar throughout the day and the presence of readily permeable renal tissue. The output of phenolsulphonphthalein in case 3 was rather high, 75 per cent in two hours. The excretion of xylose was somewhat elevated, 5.3 Gm. in twenty-four hours. These tests suggest that the kidneys in patients with continuous renal glycosuria are more permeable than they are normally, and they demonstrate in another way the low threshold in that condition.

The relationship of renal glycosuria to nephritis has been stressed by some writers.[21] Recent reviewers [22] failed to find evidence of nephritis in their patients, nor was there any evidence of nephritis in our 3 patients. According to Wearn and Richards, one might expect an increased amount of sugar in cases of nephrosis, but since a sufficient number of tubules is probably intact in that condition, normal reabsorption of sugar can occur. It is for that reason that one rarely finds glycosuria in cases of nephrosis.

The differential diagnosis between renal glycosuria and diabetes mellitus is sometimes confused by the presence of acetonuria. Numerous authors have noted the presence of acetonuria in cases of renal glycosuria, particularly following surgical intervention or during infections.[23] Acetonuria, however, may be present in association with renal glycosuria even without infection, particularly if a large amount of sugar is excreted and an insufficient amount is left in the body for the complete oxidation of fatty acids. Indeed, relative starvation can occur, as was demonstrated in case 1. Usually acetonuria is present without clinical symptoms, as in the brother of the patient in case 3, who felt perfectly well

21. Hawkins, J. A.; Mackay, E. M., and Van Slyke, D. D.: Glucose Excretion in Brights' Disease, J. Clin. Investigation **8**:107 (Dec. 20) 1929.

22. Shafton and Poncher.[20] Fanconi.[6] Marble.[7]

23. (*a*) Fowler, A. F.: Renal Glycosuria, Ann. Int. Med. **7**:518 (Oct.) 1933. (*b*) Lichtwitz, L.: Ueber das Wesen der renalen Glykosurie, Klin. Wchnschr. **11**:626 (April 9) 1932. (*c*) Allan and Vanzant.[19]

although he had marked glycosuria and acetonuria. Naturally the presence of large amounts of sugar and acetone might make one suspicious of diabetic ketosis, particularly in the presence of an illness. Ordinarily the absence of clinical symptoms of diabetes would exclude that condition. The leukocyte count may aid in the differentiation. Fowler [23a] has called attention to this differential point. Usually in a case of diabetic acidosis the leukocyte count is markedly elevated, whereas in one of renal glycosuria with acidosis the leukocyte count is low; in case 3 it was 11,000.

At another time [24] attention was drawn to the frequency of pentosuria in childhood. Seven other instances of that condition have been encountered in our outpatient department since the publication (1929) of that report. Pentosuria probably occurs frequently but is overlooked because it may cause only a slight reduction of Benedict's solution. This fact is mentioned because some of the reports of nondiabetic glycosuria in the literature do not mention the fact that the urinary reducing substance was proved to be dextrose. Indeed, in 2 of the cases of pentosuria previously described [24] the patients were considered to have had renal glycosuria, and 2 were being treated for diabetes. A serious diagnostic error must be avoided by proper chemical analysis. Once the presence of glycosuria has been established, one must differentiate by means of the history, subsequent course and proper interpretation of the results of the dextrose tolerance test between nondiabetic and diabetic glycosuria.

SUMMARY

Three cases of nondiabetic glycosuria have been described, the first 2 being examples of intermittent glycosuria in which sugar appeared in the urine only when a relatively high renal threshold was exceeded. In the third case there was a low renal threshold; therefore, constant glycosuria without hyperglycemia was present. In the latter case glycosuria occurred even when the blood sugar had fallen to 60 mg. Because of the low threshold the glycosuria was much greater than in the first 2 cases. Except for acetonuria there were no other symptoms of diabetes mellitus, such as thirst, loss of weight or polyuria, in these 3 cases, and there was no evidence that the metabolism of carbohydrate was at fault.

Continuous renal glycosuria is only a descriptive term. The question as to whether the glycosuria is continuous or intermittent is dependent solely on the threshold level of a particular patient. The true diagnostic criteria for renal glycosuria are the benign nature of the glycosuria, the typical blood sugar curves, with the exceptions noted, and a normal

24. Fischer, A. E., and Reiner, M.: Pentosuria in Children with Laboratory Data on Four Cases, Am. J. Dis. Child. **40**:1193 (Dec.) 1930.

respiratory quotient.[25] It has been shown that a high blood sugar curve (case 1), indicating a temporary loss of tolerance, can occur even in renal glycosuria.

The prognosis of continuous or low threshold renal glycosuria as noted by numerous authors [26] is excellent. Diabetes mellitus has not developed in patients who have been observed for years. The cases in which there is a higher threshold also have a good prognosis.

It seems unnecessary to separate arbitrarily the two types of renal glycosuria, for they are benign, frequently familial, and have a similar clinical picture differentiated only by the height of the threshold.

Even the type of renal threshold appears to be an inherited characteristic.

No treatment of renal glycosuria is required. Frequent meals of a somewhat higher caloric intake than normal are suggested in order to replace the food and energy lost by glycosuria and by the incomplete oxidation of fat.

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25. Rabinowitch, J. M.: Simultaneous Respiratory Exchange and Blood Sugar in Diabetic and Non-Diabetic Individuals, J. Clin. Investigation **2**:143, 1926. Paullin, J. E.: Glucose Utilizations in Renal Glycosuria, Arch. Int. Med. **37**:88 (Jan.) 1926.

26. Holst.[5] Marble.[7] Faber.[13]

PATHOGENESIS OF THE LAURENCE-BIEDL SYNDROME

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CHICAGO

The familial incidence of certain rare diseases suggests that heredity must play a decisive part in their causation. Unfortunately, however, many characters with which one must deal in the application of human genetics to the study of disease are complex and do not clearly segregate. Unit characters cannot be identified as the basis for symptoms and physical findings unless they segregate in numerical proportions compatible with the mendelian hypothesis.

One interesting disorder of familial occurrence is the Laurence-Biedl syndrome. The cardinal characteristics of this symptom complex are obesity, genital dystrophy, mental deficiency, retinitis pigmentosa and polydactylism. The syndrome typically occurs in several members of a fraternity, while other members are normal. The familial incidence of this syndrome suggests that it is a hereditary disorder, and this presumption is strengthened by the known hereditary occurrence of mental deficiency, retinitis pigmentosa and polydactylism.

Reilly and Lisser [1] were able to collect from the literature twenty-five cases of the complete Laurence-Biedl syndrome; ten of a questionably complete syndrome; twenty-seven of a partially complete syndrome, one of which was questionable, and fifteen doubtful cases. Several cases have been reported since the publication of this paper. The following case appears to be a classic member of the group.

REPORT OF A CASE

J. M., a white boy aged 11 years, was referred to the Institute for Juvenile Research because of mental retardation. There was a history of mental deficiency, obesity, polydactylism and night blindness. After examination at the Institute he was admitted for study to the pediatric service of the Research and Educational Hospital.

From the Illinois Institute for Juvenile Research and the Department of Pediatrics, University of Illinois College of Medicine.

1. Reilly and Lisser: Laurence-Moon-Biedl Syndrome, Endocrinology **16**: 337, 1932.

Family History.—The patient's parents were born in Ireland. In 1919, three years previous to the birth of the patient, the father had an attack of "flu," and at the time of the patient's examination was afflicted with parkinsonism, changes in personality, irritability and alcoholism. There was no history of obesity, polydactylism, mental deficiency or defective vision or hearing on either side of the family. There was a history of spontaneous abortion in the second month of the first pregnancy. Twin boys, the product of the second pregnancy, died at the age of 6 months of nutritional upset. The third pregnancy resulted in a girl, who died shortly after birth of a congenital deformity of the spine. The patient was the product of the fourth pregnancy. Two sisters born subsequently are normal. The mother was 32 and the father 31 at the time of the patient's birth.

Birth and Developmental History.—The delivery was normal and at full term. The patient at birth presented unilateral polydactylism on the left side—six fingers and six toes. He weighed 9½ pounds (4,309.1 Gm.). The first tooth erupted at the age of 4½ months; the child walked at 13 months and began to talk in sentences at 23 months. When he was about 1½ years of age, his mother noticed that he was retarded in development as compared with other children of his age and that he was becoming abnormally fat. At the age of 23 months his mother took him to the Children's Memorial Hospital because of constant drooling. Through the courtesy of Dr. Brennemann, we were able to obtain accurate information of that examination. At that time the patient was an obese child, weighing 34¾ pounds (15,462.3 Gm.); he appeared subnormal and showed evidence of polydactylism and undescended testicles. He was referred to the neurologic department for further study, but the mother did not return. The subsequent development was slow, and the patient continued to gain weight.

When the patient was 2 years of age his mother noticed that his eyes "looked different from other children's." He would run into objects at night unless he was led. This tendency persisted. He had never learned to read or write but was advanced to the third grade to prevent his becoming sensitive about his dulness. He had no desire to play with other children, although there was no gross disturbance of behavior.

Examination.—The patient was an obese boy of about the normal height for his age (fig. 1). The weight was 46.7 Kg. The temperature and respiratory rate were normal. The pulse rate varied from 78 to 92 per minute. The systolic blood pressure varied from 110 to 135 and the diastolic from 65 to 80. The positive findings consisted of obesity of the Fröhlich type, undescended testicles, hypogenitalism, evidence of polydactylism on the left side and mental deficiency. The extra finger had been removed surgically. The sixth toe fused with the fifth. The results of the special examinations were as follows:

Examination of the Fundi: The eyegrounds were tessellated, the central pigment coarsely granular and the equatorial region bleached. The retinal vessels were markedly contracted. The findings were consistent with those of atypical retinitis pigmentosa.

Basal Metabolism Tests: The basal metabolic rates were + 1, + 10, + 2 and + 6 per cent (Benedict standard).

Chemical Examination of the Blood: The dextrose content was 111 mg. per hundred cubic centimeters of plasma; the result of the glucose tolerance test was normal; the nonprotein nitrogen content was 29 mg. per hundred cubic centimeters of plasma, and the cholesterol content, 259 mg.

Serologic Tests: The Wassermann and Kahn tests were negative.

Urinalysis: The results of the tests and the volume were normal.

Measurements: The occipitofrontal circumference of the skull was 54 cm.; the span of the arms, 144 cm.; the circumference of the chest (at the level of the nipples), 79 cm.; the circumference of the abdomen (at the level of the umbilicus), 79 cm.; the length from the vertex to the symphysis pubis, 69 cm.; the length from the symphysis pubis to the heel, 74 cm.

A roentgenogram of the skull and the centers of ossification revealed normal conditions.

Psychometric Examination: On a Stanford-Binet examination the patient attained the rating of a mental age of 6 years and 8 months, which with his chronological

Fig. 1.—Photograph of the patient in our case, showing the dull expression, mammary, girdle and mons type of obesity, hypogenitalism and polydactylism and syndactylism of the left foot.

age of 11 years and 1 month gave him an intelligence quotient of 61. The classification was that of high grade mental deficiency. In his performance on the Herring-Binet test he achieved the rating of a mental age of 6 years and 7 months and an intelligence quotient of 58; the classification was that of high grade mental deficiency.

His score on a point performance test was below the 6 year level at which the norms begin. A definite intelligence rating based on this test was therefore impossible, although his intelligence quotient necessarily would have been below 55. He

displayed poor comprehension of spatial relations as well as poor motor performance in simple tasks.

In his behavior he was a dull, slowly reacting, relatively unsocial boy, apparently conscious of his retardation.

In a second Stanford-Binet examination when 11 years and 11 months old, the patient achieved a mental age of 7 years, giving him an intelligence quotient of 59. This is in close agreement with the rating of 61 obtained before treatment was instituted.

Course in the Hospital.—The patient was given intramuscularly 1 cc. of solution of anterior lobe pituitary extract and 4 minims (0.24 cc.) of solution of posterior lobe pituitary extract daily for one month and then three times a week for four months. Administration of thyroid extract was started in doses of 2 grains (0.12 Gm.) twice a day after the patient had been given anterior lobe pituitary extract for one month. After the patient had been given anterior lobe pituitary extract for about two weeks the testicles were palpated in the scrotum. Otherwise, no definite change has been noted in the patient's condition under this therapy to the time of writing.

COMMENT

Numerous theories have been held as to the cause of the Laurence-Biedl syndrome since it was first described by Laurence and Moon in 1866.[2] For the most part, the theories are concerned with an attempt to explain adiposogenital dystrophy. The most generally accepted hypothesis prior to the last few years was that sponsored by Biedl[3] and Raab.[4] Biedl suggested that the syndrome is a familial form of dystrophia adiposogenitalis of cerebral rather than of pituitary origin, and Raab in Biedl's clinic attempted to elucidate the abnormal physiologic condition. Raab suggested that the symptom complex resulted from a dysfunction of the hypothalamic centers caused by a blocking off of secretion from the pars intermedia by a high and massive dorsum sellae. While the point made by Biedl is now generally accepted, there are many objections to Raab's explanation, one of the most important of which is the fact that an abnormal sella is not present in all the cases reported.

The recent trend is toward the explanation of the pathogenesis of the syndrome on the basis of a hereditary developmental defect.[5] Ornsteen ascribed the four most constant phenomena of the syndrome—genital dystrophy, obesity, mental deficiency and retinitis pigmentosa to a common cause, namely, a segmental embryonic deficiency in the development of the brain. He explained adiposogenital dystrophy of the Laurence-

2. Laurence, J. Z., and Moon, R. C.: Brit. Ophth. Rev. **2**:32, 1866.

3. Biedl, A.: Deutsche med. Wchnschr. **48**:1630, 1922.

4. Raab, W.: Wien. Arch. f. inn. Med. **7**:443, 1924.

5. (*a*) Timme, W.: Heredity, A. Research Nerv. & Ment. Dis., Proc. **3**:6, 1925. (*b*) Rieger, H., and Trauner, R.: Ztschr. f. Augenh. **68**:235, 1929. Ornsteen, A. M.: Am. J. M. Sc. **183**:256, 1932.

Biedl syndrome as an embryonal defect involving the diencephalon. The genes concerned with the evolution of this region of the brain "are abnormal and are transmitted through the germ plasm producing an inherited diencephalic defect as a unit character." The almost constant association of retinitis pigmentosa and mental deficiency with the Fröhlich syndrome in this disorder is explained on the basis of a genetic defect of the forebrain or prosencephalon. The ventral segment of the ectopic zone of this region gives rise to the infundibulum, optic chiasm and retinal fibers. Ornsteen pointed out, therefore, that a defect in the character of the genes responsible for the development of this region may produce an infundibular defect which gives rise to Fröhlich's syndrome; the chiasmatic defect may produce optic atrophy, and the involvement of certain fibers in the optic chiasm may result in pigmentary degeneration of the retina. The defect in intellectual development is part of this segmental embryonic deficiency, but it involves the cephalic segment of the ectopic zone. Thus he concluded that "the adiposogenital dystrophy, retinitis pigmentosa and mental deficiency are related to a genetic defect of the ectopic zone (primitive forebrain or prosencephalon) in its cephalic and ventral segments, in other words a cerebral genotypic unit character." Polydactylia, deformities of the skull, atresia ani and other anomalies occasionally encountered were attributed to the accidental coupling of somatic genotypic unit characters.

While this theory sounds plausible the explanation that accidental coupling of the genes is responsible for the other components of the syndrome may be challenged on the ground that it puts too great a strain on probability. In the cases collected by Reilly and Lisser, polydactylism was present in forty-two cases and absent in twenty-six, and the presence or absence was unstated in nine cases. If these cases are enumerated by families, polydactylism was present in thirty-three families and absent in fifteen, and the presence or absence in nine families was unstated. In view of the extremely low incidence of polydactylism in the population, this explanation puts an intolerable load of coincidence on "accident." It may be further noted that syndactylism occurred in five of the patients and in five of the families with polydactylism and in three of the persons and in three of the families without polydactylism.

It should furthermore be pointed out that within families polydactylism is associated with the Laurence-Biedl syndrome. For instance, in the family reported on by Ricaldoni and Isola,[6] four children presented the Laurence-Biedl syndrome including polydactylism, and four were normal and had no polydactylism. This does not look like an association

6. Ricaldoni, A., and Isola, A.: Bull. et mém. Soc. méd. d. hôp. de Paris **52:** 131, 1928.

based on chance. Within thirty-five families for which there is adequate information, thirty, or 58 per cent, of fifty-two persons affected with the Laurence-Biedl syndrome or a related disturbance had polydactylism, while only twelve, or 15 per cent, of their one hundred and twenty-five siblings had polydactylism. The likelihood of obtaining such a disparity on the basis of chance is negligible.

Solis-Cohen and Weiss [7] reported two cases of the complete syndrome occurring in eight siblings, while two other children presented all the characters but polydactylism. Occasionally polydactylism may involve persons in these families otherwise unaffected. For instance, Biedl and Raab reported the complete syndrome in a boy of 16 and a sister of 22. Two other children among the eight siblings exhibited polydactylism without the other signs of the syndrome.

It may be concluded that the hypotheses presented heretofore are inadequate to explain the phenomena of the Laurence-Biedl syndrome. The most nearly adequate is that of Ornsteen, which furnishes a working hypothesis for the occurrence of the adiposogenital dystrophy, the mental deficiency and the retinitis pigmentosa but does not offer an adequate explanation for the occurrence of the polydactylism or of the other defects occasionally associated with this syndrome.

In proceeding to the formulation of a new hypothesis, it is well to begin with the fact that one is dealing with a familial and presumably hereditary syndrome—presumably hereditary because heredity is known to be the major factor in the occurrence of most of the component characteristics when they appear in isolation from the others. Without going into a general discussion of the mendelian theory it may be well to consider briefly some of the known facts of mendelian heredity. While these processes have not actually been proved for the germ cells of man, there seems to be no reason to suppose that they do not occur in man in the same way in which they have been observed to occur in the lower forms of life.

The fourth law of heredity may be stated thus: "Characters whose genes are located in the same chromosome are linked in heredity." [8]

Linkage has been well worked out in the case of the vinegar-fly (Drosophila). For example, black color has been found in some strains to be linked with the vestigial character of the wings. In the event of mating a black-bodied vestigial-winged fly with a gray-bodied fly with normal wings and of further intermating the offspring of this cross, it is found that the flies which hatch with black bodies typically have vestigial wings, and the flies which hatch with gray bodies typically have normal wings. The explanation given is that the genes for black

7. Solis-Cohen, S., and Weiss, E.: Am. J. M. Sc. **169**:489, 1925.

8. Burlingame, L. L.; Heath, H.; Martin, E. G., and Pierce, G. J.: General Biology, New York, Henry Holt & Company, Inc., 1923, p. 364.

color and those for vestigial wings, being located in the same chromosome, are either both eliminated or both retained in the reduction division.

This same explanation can readily be invoked to explain the coincidence of polydactylism with the other elements of the Laurence-Biedl syndrome which Ornsteen ascribed to a unit character.

The fifth law of heredity is as follows: "Linked genes may cross over from one chromosome of a pair to its mate by exchange of corresponding segments of paired chromosomes."[9] This occurrence is diagrammatically illustrated in figure 2.

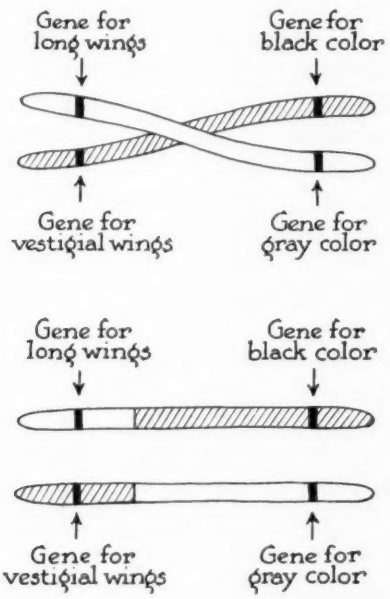
Gene for long wings
Gene for black color
Gene for vestigial wings
Gene for gray color
Gene for long wings
Gene for black color
Gene for vestigial wings
Gene for gray color

Fig. 2.—Diagrams illustrating the manner in which crossing over may occur during the stage of synapsis.

During the stage of synapsis in the process of mitosis, the paired chromosomes are associated side by side and often twisted. Apparently during this stage they may exchange segments after the fashion indicated in the diagram.

Thus in some cases, in the experiment in mating already outlined, black flies with long wings or gray flies with vestigial wings may be hatched. The frequency of crossing over depends on the distance between the genes on the paired chromosomes, and in a large number of instances in the case of the vinegar-fly these distances have been calculated mathematically and proved by their interrelations.

9. Burlingame,[8] p. 374.

An adequate explanation is now offered for the failure of the uniform appearance of polydactylism among patients with the Laurence-Biedl syndrome, as in the family reported by Solis-Cohen and Weiss, and for its appearance in otherwise unaffected members of the family. The condition may occur because of a crossing over of the genes determining polydactylism.

Since the gap has been satisfactorily bridged between the genital, obese, retinal and mental aberrations and polydactylism, one is no longer under such pressure as was Ornsteen to account for the first group of characteristics on a unitary basis. The knowledge of Fröhlich's syndrome and of the intimate relations (anatomically at least) between the weight-controlling and the gonad-stimulating center leads one to postulate a relationship in causality between the two conditions. The association with retinitis pigmentosa is less evident, although anatomically and in particular embryologically it is, as Ornsteen has pointed out, closely connected. But when nerve deafness is seen to appear as a substitute for retinitis pigmentosa in two members of a family [10] with this syndrome, one may well be somewhat disturbed with this explanation in view of the anatomic and embryologic discontinuity of the hypothalamus and the acoustic nerve. Furthermore, deafness is frequently reported both in patients with the Laurence-Biedl syndrome [11] and in patients and even in families of patients afflicted with retinitis pigmentosa alone.[12]

More probable than the explanation given by Ornsteen seems a linkage between at least three genetic factors—one responsible for obesity and genital dystrophy, one for retinitis pigmentosa and one for polydactylism. It is a fair speculation whether or not mental deficiency is due to one of these genes or whether it is dependent on a linked gene. There appears to be a further genetic relationship between retinitis pigmentosa and nerve deafness. This may well be a further instance of linkage.

SUMMARY

A case of the Laurence-Biedl syndrome is reported. The various hypotheses concerning the pathogenesis are reviewed. It is impossible to account for the association of the characteristics of the Laurence-Biedl syndrome on the basis of any of the hypotheses previously advanced. A hypothesis is here presented that the syndrome is due to

10. Weiss, E.: Am. J. M. Sc. **183**:268, 1933.

11. Bonheim, F.: Endokrinologie **4**:263, 1928.

12. Nettleship, E.: Royal London Ophth. Hosp. Rep. **17**:1, 1907; **17**:151, 1908; **17**:333, 1908.

the linkage of two or more genes bearing unit character. These genes cannot carry simple dominants; they may bear simple recessives.

NOTE.—Since this article was submitted for publication, Cockayne Grestin and Sorsby (*Quart. J. Med.* **4**:93 [April] 1935) have published a comprehensive review of the subject and expressed the same opinion as ours regarding the pathogenesis. In their discussion of the pathogenesis they point out that Rieger and Trauner [5b] also expressed the belief that the parts of the syndrome based on mesoblastic and epiblastic defects are recessive and are due to mutations of two genes in the same chromosome. A similar suggestion was made independently by Cockayne (Inherited Abnormalities of the Skin and Its Appendages, London, Oxford University Press, 1933, p. 40).

Progress in Pediatrics

ELIMINATION DIETS FOR CHILDREN

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The use of so-called nonallergic diets has a definite place in pediatric work. Specialists in allergic disorders are well aware of the fact that positive reactions to scratch tests or intracutaneous tests may indicate sensitivity that has ceased to exist clinically or may be the expression of local irritation. On the other hand, negative reactions to food often exist with clinical sensitivity. The latter phenomenon is explained by certain allergists as occurring primarily in those cases in which clinical reactivity follows by a relatively prolonged latent interval exposure to the offending substance. Whatever the explanation of these disconcerting events, the indication for the use of trial diets is apparent and has been stressed by Rowe,[1] Hopkins, Waters and Kesten [2] and Waters.[3] The efficacy of the correctly selected diet is attested by these authors' reports of numerous therapeutic successes.

A thorough knowledge of the various ingredients of common foodstuffs is not obtainable by the practicing physician without considerable inconvenience; nor is he likely to select for trial diets foods least prone to cause allergic disturbance without special study of the literature and personal experience with atopic disorders. Yet there have not appeared in any pediatric periodical elimination diets designed for the physician's use. For the past year in the clinic for the treatment of allergy in children of the New York Hospital and in private practice, diets which I prepared for patients with allergy have been employed with satisfactory results.

Recipes have been obtained from the reprints of the authors just quoted, from menus published by a commercial food company,[4] from

From the clinic for the treatment of allergy of the Department of Pediatrics, the New York Hospital, and the Cornell University Medical College.

1. Rowe, A. H.: (*a*) Food Allergy, J. A. M. A. **91**:1623 (Nov. 24) 1928; (*b*) Gastro-Intestinal Allergy, ibid. **97**:1440 (Nov. 14) 1931.

2. Hopkins, J. Gardner; Waters, Irene, and Kesten, Beatrice: Elimination Diets as an Aid in the Diagnosis and Treatment of Eczema, J. Allergy **2**:239 (May) 1931.

3. Waters, Irene: Elimination Diets for the Diagnosis and Treatment of Food Allergy, J. Allergy **2**:225 (May) 1931.

4. Special Recipes, Menus and Food Lists from Wheat, Egg, and Milk-Free Diets, St. Louis, Ralston Purina Company, 1932.

standard books on cookery and from Miss Mabel Stimson, dietitian of the hospital, who gave helpful suggestions. With the elimination of occasional articles, obvious to the pediatrician, these diets are considered suitable for the average infant of about 1 year.

The seven diets may be roughly classified as follows:

Diets 1 and 2: without milk, egg and wheat
Diet 3: without egg and wheat, with milk
Diet 4: without egg and milk, with wheat
Diet 5: without milk
Diet 6: without wheat
Diet 7: without egg

It is believed [1a] that in some patients sensitization to whole groups of foods, as to fruits, cereals, meats or vegetables, may exist. With the aid of the type diets the resourceful physician may improvise special lists to meet this contingency. An exclusive diet of milk, 2 or 3 quarts (1.9 to 2.8 liters) daily, may be used for the test period if there are no indications of sensitization to milk and if a trial of other diets has failed.

The seven type diets have been compiled from a pediatrician's point of view. They represent a definitely wider choice of type diets for children than have previously been published.

FOODS AND ALLERGY

That eczema, angioneurotic edema, asthma, vasomotor rhinitis and urticaria are frequently due wholly or in part to food in sensitized persons is too well known to require discussion. Polymorphic digestive disturbances have been attributed on good evidence to allergy.[1b] I am familiar with the case of a patient with nonspecific ulcerative colitis which was seemingly dependent on intolerance to all fruits who was clinically cured by their elimination. Some cases of migraine and, rarely, even of epilepsy seem to have an atopic etiology. Certain rashes, other than eczema, caused by food are fairly common. Sinusitis secondary to vasomotor rhinitis and asthma apparently of infectious origin may sometimes be shown to originate in the use of foods to which the patient is sensitized and be completely cured by the elimination of those foods.

Cooke's [5] statistics emphasized the great importance of foods as excitants in the first five years of life, especially in the first three years, when there is a probability that sensitization to food exists alone. Stuart and Farnham [6] found that by far the greatest sensitivity to food is encountered in the second year of life. Thereafter there is a rapid

5. Cooke, Robert A.: Asthma in Children, J. A. M. A. **102**:664 (March 3) 1934.

6. Stuart, H. C., and Farnham, H.: Acquisition and Loss of Hypersensitiveness in Early Life, Am. J. Dis. Child. **32**:341 (Sept.) 1926.

decline; after the sixth year the incidence is low. They emphasized the now well known changing sensitivity of early childhood and repeated the cutaneous tests every six months. Chobot [7] found that the incidence of sensitivity to inhalants and that of sensitivity to foods, as shown by cutaneous reactions, were parallel until the ninth year, when inhalants definitely established themselves as the predominating causes in the cases studied.

SELECTION OF AN APPROPRIATE TRIAL DIET

In order to detect specific offending foodstuffs, a carefully taken history may be of distinct value. The physician should attempt to discover foods the child dislikes or the ingestion of which causes abdominal pain, vomiting, diarrhea or the more common allergic reactions. If the disorder is periodic and the child has symptom-free intervals the "food diary" may be useful. Daily notation is made of everything which passes the patient's lips, and the time of onset and cessation of any allergic manifestations is charted. In this manner one or more foods may be proved to be followed with more or less regularity by clinical upset.

Scratch or intracutaneous tests prove valuable in a fair proportion of cases, but should be interpreted by one experienced in their use and in interpreting their significance. In the event of the child's skin being unsuited for cutaneous tests, whether from general hyperirritability to test substances or because of extensive dermatitis, the tests by so-called passive transfer [8] have sometimes revealed important information. In connection with the cutaneous tests I feel it worth while to point out that in eczema, especially of the "flexural type," patch tests with the common inhalants, as described by Peck and Salomon [9] may show the condition to be due to these substances acting as contactants. In such situations, therefore, such tests should probably be included in the investigation. In the clinic for the treatment of allergy in children at the New York Hospital, somewhat limited experience with the patch test in the "flexural type" of eczema has, however, been disappointing. Further investigation in this particular field should be pursued. On the other hand, patients who give negative reactions to food tests but in whom there is a sensitivity to inhalants not controlled by suitable procedures are subjects for treatment with elimination diets.[5]

Assuming that one has reason to suspect one or more foods to be the cause of the patient's atopy, one may select diet 3, 4, 5, 6 or 7, with

7. Chobot, Robert: Asthma in Children, Am. J. Dis. Child. **45**:25 (Jan.) 1933.

8. Walzer, M., and Kramer, S. D.: Indirect Method of Testing for Conditions of Atopic Sensitiveness, J. Immunol. **10**:835 (Sept.) 1925.

9. Peck, Samuel M., and Salomon, Gustav: Eczema of Infancy and Childhood, Am. J. Dis. Child. **46**:1308 (Dec.) 1933.

or without modification, as indicated. A trial period of two or three weeks is pursued. If progressive improvement or freedom from symptoms is secured, a new food may be added every fourth day and may be given at least once a day after this time. If a recrudescence of signs or symptoms occurs the suspected food should be eliminated at once and tried at a subsequent date. In this fashion injurious foods may be separated and withheld. In some cases prolonged abstinence from such foods may result in desensitization.[1a] In a few cases desensitization has apparently been accomplished by the use of the specific peptones of Luithlen and Urbach.[2] In others desensitization sometimes occurs when gradually increasing amounts of the offending food are added over the course of several months, starting with minute amounts.[10] In older children the injection of foods for a long period has been tried by Cooke.[5] A discussion of these types of therapy is not within the scope of this article.

If the trial of diets 3 to 7 fails to give satisfactory results one is justified in assuming that injurious food or foods are being ingested. I then turn to diet 1 or 2 and experiment with its effect. If the first diet fails to give the desired results the other is tried. Initial attempts with diets 1 and 2 are indicated when a study of the case gives indefinite information with regard to possible offending foods. If diets 1 and 2 are ineffective, nothing remains but to place the patient on an exclusive diet of milk or to devise special diets which exclude an entire group of foods, such as all cereals, meats, vegetables or fruits. Fortunately such group idiosyncrasies are relatively uncommon and may sometimes be demonstrated by the skin tests.

THE DIETS

In order to make this article as lucid, practical and simple as possible, each diet will be given in its entirety. This procedure entails the repetition of certain recipes and instructions, which seems justified in view of the added convenience and the extra assurance of avoidance of errors and omissions in the practical following of these diets and which simplifies the physician's duty of going over the diet carefully with whoever is responsible for its observance.

Both in private practice and in work at the clinic, to each diet is added the following brief exposition on the ingredients of certain commonly used foods:

To be effective, a diet must be followed in the strictest manner. A minute amount of forbidden foodstuff may cause as much damage by its ingestion as a very large amount. For the sake of greater variety corn flakes and Post Toasties may be included in diet 1, though malted barley is contained in both these cereals

10. Schloss, O. M.: Allergy in Infants and Children, Am. J. Dis. Child. **19**: 433 (June) 1920. Rowe.[1a]

and the addition of barley must be recognized as an extra factor which may not be desirable. Otherwise, the corn cereal must be limited to corn-meal. On the other hand, if corn is excluded, ordinary brands of viosterol, which are put up in a base of corn oil, must not be used, but Abbott's or Winthrop's viosterol, which have a sesame oil base, is permitted. Patients who are sensitive to milk must avoid butter, butter-containing foods and those cooked in butter, as well as white bread, macaroni, malted milk and a host of other innocent-appearing preparations. The common egg-containing foodstuffs are listed in diet 7. Symptoms in a person with a sensitivity to eggs have been reported to appear after moistening with the lips a paint brush dipped in tempora paint, which contains egg.[11] If wheat is interdicted, gravies, stews and soups thickened with wheat flour must be avoided as well as such common articles as noodles, macaroni, pie-crusts, many breakfast foods, pancake flours, meat or poultry stuffings, muffins and yeast-cakes.

These and other foods may appear in an amazing number of forms. The diet is designed to protect the patient from eating possible unsuspected offenders. Therefore, rigid adherence to it is vital.

For a fairly broad summary of the composition of common articles of food one may refer to a textbook.[12]

Diets 5, 6 and 7, though relatively liberal, contain certain arbitrary restrictions. These can be more readily justified on the grounds of a possible psychologic advantage than for any scientific rationale. A combination of diets 1 and 2 is sometimes desirable.

It is well to have a detailed record made of everything the patient eats. In this way an infraction of the diet may be detected. It is also well to weigh weekly the patients on the more restricted schedules.

DIET 1 (WITHOUT MILK, EGG OR WHEAT)

Beverage		
	Pineapple juice	
Cereal		
	Corn-meal	Post Toasties
	Hominy	Samp (this is expensive)
Fruit		
	Pineapple	Apricots
	Apple	
Fish		
	Not allowed	
Meat		
	Lamb	Lamb chops
	Mutton	Lamb's kidneys
Vegetable		
	Corn (for child of 6 years or older) fresh or canned	Asparagus, fresh or canned
		Lettuce

11. Spain, W. C.: Food Hypersensitiveness, New York State J. Med. **33**:1100 (Sept. 15) 1933.

12. Coca, A. F.; Walzer, M., and Thommen, A. A.: Asthma and Hay Fever in Theory and Practice, Springfield, Ill., Charles C. Thomas, Publisher, 1931.

Bread

Corn pone
Corn crisps

Butter Substitute

Salted yellow petrolatum

Fat

Mazola oil

Flour Substitute

Corn-starch

Miscellaneous

Karo
Apricot jam
Molasses
Refined sugar
Brown sugar
Salt
Baking soda
Unflavored gelatin
Hard candy, flavored with peppermint, wintergreen or cinnamon (no soft candy)
Viosterol
Lactose

1. No foods other than those specified can be used. Thus, gravy for the lamb may be thickened with corn-starch and not with flour; corn-meal may be fried only in Mazola.

2. The foods permitted may be eaten in unlimited quantities.

3. Even a minute amount of food not included in the diet may, if eaten, nullify an otherwise successful trial and confuse the solution.

4. Combinations and preparations of the foods included in the diet may be devised by the patient.

5. To prevent constipation a liberal use of the fruits permitted is advisable. In addition, water should be drunk in large quantities, and brown sugar on the cereals may be helpful.

6. Viosterol, but not cod liver oil, may be taken if ordered.

RECIPES FOR DIET 1

Corn Crisps

½ cup corn-meal
½ teaspoon salt
1 cup boiling water

Add boiling water to the salt and corn-meal and stir until smooth. Drop from a spoon onto a baking sheet which has been greased with Mazola oil. Bake in a hot oven until brown. The crisps should be very thin and small. Salted yellow petrolatum may be used as a substitute for butter.

Corn Pone

½ cup corn-meal
½ cup boiling water
½ teaspoon salt

Add boiling water to the salt and corn-meal and mix thoroughly. Shape the dough with the fingers, making oval pones ½ inch (1.2 cm.) thick. Place on a baking sheet which has been greased with Mazola oil and bake in hot oven. Serve with Karo or molasses.

Indian Pudding

2 tablespoons corn-meal
1 tablespoon sugar
¼ teaspoon salt
1 cup water
1 tablespoon molasses

Cook the corn-meal in water in a double boiler for twenty minutes. Add molasses, salt and sugar. Put in a baking pan which has been greased with Mazola oil. Set in a pan of water and bake forty minutes in a slow oven. Serve with Karo.

Apricot Gelatin

1 teaspoon gelatin
¼ cup boiling water
Pinch of salt
2 tablespoons cold water
¾ cup apricot juice
¼ cup sugar

Soak gelatin in cold water five minutes and dissolve in boiling water. Add sugar and stir until dissolved; then add salt and apricot juice. Pour in mold, first dipped in cold water, and chill.

Pineapple Drink

Canned pineapple juice, iced, with 3 tablespoons of lactose and cane sugar added to taste. Serve in an ordinary tumbler.

Brown Sugar Candy

1 cup brown sugar
¼ cup water
Pinch of salt

Mix sugar, water and salt and cook until it forms a soft ball when dropped in cold water. Remove from the fire and cool. Beat until creamy.

French Dressing

Mazola or mineral oil should be substituted for olive oil. Vinegar may be used in this diet.

Hominy Grits

1 cup hominy
1 teaspoon salt
4 cups water

Wash the hominy several times in cold water. Soak over night. Cook for one hour.

Fried Hominy Grits

Pour the left-over hominy in a shallow pan and put on ice to become firm. Cut out round cakes with a biscuit cutter and fry in Mazola oil. Serve with Karo or molasses as a dessert.

Samp

½ cup samp
1 teaspoon salt
4 cups water

Prepare in the same way as hominy grits, but boil for five or six hours.

Pineapple Ice

½ cup confectioner's sugar
3 cups water
3 cups pineapple juice

Dissolve the sugar in the water and add the pineapple juice. Pour into the freezer. Pack with ice and salt. When frozen, remove from the freezer. Pack in a mold. Pack again in salt and ice until ready to serve. (Commercially prepared pineapple sherbet should not be used. It usually contains lemon and egg-white.)

SUGGESTED MENUS FOR DIET 1

Breakfast: Apricots, baked apple, apple sauce
Corn-meal, hominy, Post Toasties, samp with apricot juice, Karo or molasses
Corn crisps, corn pone with salted yellow petrolatum and Karo or molasses
Corn-meal mush with Karo or molasses
Pineapple juice

Lunch: Lamb broth
Lamb, lamb chops, lamb's kidneys, mutton and gravy made with cornstarch, not flour
Corn crisps or corn pone
Corn, asparagus or lettuce (with or without special French dressing)
Indian pudding, apricots, baked apple, apple sauce, raw scraped apple, pineapple ice, apricot gelatin, fried hominy grits with Karo or molasses
Brown sugar candy
Pineapple juice

3:30 p. m.: Pineapple drink

Supper: May be selected from the lists for breakfast and lunch. The age of the patient chiefly determines the choice. Viosterol may be included if ordered.

DIET 2 (WITHOUT MILK, EGG OR WHEAT)

Fruit

Prunes	Grapes
Plums	

Beverage

Grape juice

Cereal

Rice	Puffed Rice
Rye	Rice Krispies

Fish

Not allowed

Meat

Beef

Vegetables

String beans	Carrots

Bread

Ry-Krisp (Ralston-Purina Company)	100 per cent whole rye bread [13]
	Rye-rice muffin

Butter Substitute

Salted Crisco

Fat

Crisco

Flour Substitutes

Rice flour	Rye flour

13. Most rye breads contain wheat and must not be ordered unless specifically known to be wheat-free.

Miscellaneous

Maple syrup
Syrupy glucose
Royal, Snow King or any other baking powder which according to the label on the can does not contain egg
Baking soda
Salt
Refined sugar
Gelatin (unflavored)
Brown sugar
Hard candy flavored with peppermint, wintergreen or cinnamon (no soft candy)
Lactose
Molasses
Abbott's or Winthrop's viosterol

1. No foods other than those specified can be used. Thus, gravy for the beef may be thickened only with rye flour or rice flour and with no other. Frying may be done only in Crisco.

2. The foods permitted may be eaten in unlimited quantities.

3. Even a minute amount of food not included in the diet may, if eaten, nullify an otherwise successful trial and confuse the solution.

4. Combinations and preparations of the foods included in the diet may be devised by the patient.

5. To prevent constipation a liberal use of the permitted fruits is advisable. In addition, water should be drunk in large quantities, and brown sugar on cereals may be helpful.

6. Abbott's or Winthrop's viosterol may be taken if ordered. Other brands of viosterol or cod liver oil must not be used in this diet.

RECIPES FOR DIET 2

Plum Gelatin

1 teaspoon gelatin
2 tablespoons cold water
¼ cup boiling water
¾ cup canned plum juice
Pinch salt

Follow directions for making grapefruit gelatin in diet 1.

Brown Sugar Candy

1 cup brown sugar
¼ cup water
Pinch of salt

Mix the sugar, water and salt and cook until the mixture forms a soft ball when dropped in cold water. Remove from the fire and cool. Beat until creamy.

Rye and Rice Muffins

⅓ cup rice flour
⅔ cup rye flour
6 teaspoons baking powder
4 teaspoons sugar
¼ teaspoon salt
⅔ cup water
½ tablespoon Crisco, melted

Sift the dry ingredients together. Add the water and melted shortening and beat thoroughly. Pour into muffin tins greased with Crisco and bake in a hot oven (400 F.). The recipe makes six muffins, 2 inches (5 cm.) in diameter.

Cinnamon Toast

4 tablespoons sugar
2 teaspoons cinnamon
4 Ry-Krisp wafers

Mix the sugar and cinnamon together. Brush the Ry-Krisp wafers with Crisco and bake in a moderate oven (350 F.) until light brown. Sprinkle with sugar and cinnamon while warm.

Gravy

2 tablespoons rye flour	1 cup beef stock or water
1 tablespoon Crisco	Salt and pepper

Blend the fat in which meat was cooked, or Crisco, with the flour. Add the meat stock slowly and stir until thick. Season with salt and pepper. This makes 1 cup of gravy.

SUGGESTED MENUS FOR DIET 2

Breakfast: Grape juice, stewed prunes, or stewed plums
Boiled rice, Puffed Rice, Rice Krispies with prune or plum juice or maple syrup
Salted Crisco
100 per cent whole rye bread
Stewed beef kidneys or liver

Lunch: Beef bouillon with rice
Roast beef, calf liver, beef liver, beef kidneys, steak
Boiled rice
String beans or carrots
Ry-Krisps
100 per cent whole rye bread
Rye and rice muffins with substitute for butter or maple syrup
Grapes, stewed plums or prunes, plum gelatin
Grape juice drink
Brown sugar candy

3:30 P. M.: Grape juice drink

Supper: May be selected from the lists for breakfast and lunch, the age of the patient determining the choice. Abbott's or Winthrop's viosterol may be included if ordered.

DIET 3 (WITHOUT EGGS AND WHEAT, WITH MILK)

Beverage

Cream, milk (whole milk, boiled for one or two hours, Smaco hypoallergic milk 300 or 302, unsweetened evaporated milk, buttermilk or goat's milk, if allergy for milk is suspected, but milk in modified form is desirable)

Cereal

Oatmeal	Rye
Barley	

Fruit

Peach	Pear

Fish

Not allowed

Meat

Lamb

Vegetable

Peas	Sweet potato

Bread

Barley-oatmeal muffin	100 per cent whole rye bread [13]
Ry-Krisp (Ralston-Purina Company)	

Fat

Butter

Flour Substitute

Rye flour	Barley flour (bought at any drugstore)

Miscellaneous

Refined sugar	Cottage cheese
Brown sugar	Unflavored gelatin
Salt	Hard candy flavored with peppermint, wintergreen or cinmon (no soft candy)
Cream of tartar	
Baking soda	
Royal, Snow King or any other baking powder which according to the label on the can does not contain egg	Simmons' arrowroot dessert (arrowroot, cane sugar, gelatin, vanillin, salt and coloring matter)
Molasses	Lactose
Molasses candy	Abbott's or Winthrop's viosterol
Cream cheese	

1. No foods other than those specified can be used.

2. The foods permitted may be eaten in unlimited quantities.

3. Even a minute amount of food not included in the diet may, if eaten, nullify an otherwise successful result and confuse the solution.

4. Combinations and preparations of the foods included in the diet may be devised by the patient.

5. To prevent constipation as much water as possible should be drunk, brown sugar may be used in place of white sugar, and large amounts of fruit and vegetables must be eaten.

6. Viosterol in sesame oil may be used. Cod liver oil is not allowed.

RECIPES FOR DIET 3

Barley-Oatmeal Muffins

⅔ cup oatmeal	½ teaspoon baking soda
⅓ cup barley flour	¾ teaspoon cream of tartar
1 tablespoon sugar	⅓ cup water
⅓ teaspoon salt	1 tablespoon butter

Mix the ingredients in the order given. Pour into muffin tins which have been greased with butter. Bake in a hot oven from fifteen to twenty minutes. If the muffins are not eaten fresh it is best to moisten them and reheat in the oven before serving.

Brown Sugar Candy

1 cup brown sugar
¼ cup water
Pinch of salt

Mix the salt, sugar and water and cook until it forms a soft ball when dropped into cold water. Remove from the fire and cool. Beat until creamy.

SUGGESTED MENUS FOR DIET 3

Breakfast: Fresh or stewed peaches, pears
Oatmeal, with milk or cream
Barley-oatmeal muffins with butter or molasses
100 per cent whole rye bread, Ry-Krisp
Glass of milk

Lunch: Lamb broth with barley
Roast lamb, lamb chops, lamb kidneys, mutton
Peas, sweet potato
Barley-oatmeal muffins with butter or molasses, 100 per cent whole rye bread, Ry-Krisp
Milk, cream cheese, cottage cheese, buttermilk
Peaches, pears, Simmons' arrowroot dessert

3:30 P. M.: Glass of milk

Supper: May be selected from the lists for breakfast and lunch according to the age of the child

DIET 4 (WITHOUT MILK AND EGG, WITH WHEAT)

Fruit

Peaches
Prunes
Pineapple

Beverage

Pineapple juice

Cereal

Farina
Cream of wheat
Wheatena
Wheatsworth
Puffed Wheat
Shredded Wheat

Meat

Roast beef
Calf liver
Beef liver
Beef kidneys
Steak
Scraped beef

Vegetables

Onion
Carrots

Bread

Whole wheat bread[14]
Uneeda Biscuit (National Biscuit Company)[15]
Graham crackers (National Biscuit Company)

14. Some whole wheat breads contain milk. Whole wheat bread is allowed in this diet only when the brand specifically ordered is known to be made without milk.

15. Only Uneeda Biscuits and graham crackers made by the National Biscuit Company and other brands which are known not to contain milk and/or egg may be used.

Butter Substitute

Salted yellow petrolatum
Salted Crisco

Fat

Beef suet or fat
Crisco
Wesson Oil

Miscellaneous

Spaghetti made without milk (this does not include macaroni or noodles)
Wheat flour
Sugar
Salt
Unflavored gelatin
Hard candy flavored with peppermint, wintergreen or cinnamon
Cream of tartar
Baking soda
Royal, Snow King or any other baking powder which according to the label on the can does not contain egg
Molasses
Crisco
Syrupy glucose
Wesson Oil
Lactose
Abbott's or Winthrop's viosterol

1. No foods other than those specified can be used.

2. The foods permitted may be eaten in unlimited quantities.

3. Even a minute amount of food not included in the diet may, if eaten, nullify an otherwise successful trial and confuse the solution.

4. Combinations and preparations of the foods included in the diet may be devised by the patient.

5. To prevent constipation a liberal use of the permitted fruits is advisable. In addition, water should be drunk in large quantities, and brown sugar on cereals may be helpful.

6. Abbott's or Winthrop's viosterol may be used in this diet. Cod liver oil is not permitted.

7. Only specified brands of bread may be used; others usually contain milk. Crackers other than those specified may contain milk or egg.

RECIPES FOR DIET 4

Home-Made Biscuits

1 cup wheat flour
¾ teaspoon cream of tartar
½ teaspoon baking soda
½ cup water
1½ tablespoons Crisco
¾ teaspoon salt

Mix and sift dry ingredients. Rub in Crisco with two knives or a fork. Add water. The dough may be dropped from a spoon to a pan greased with Crisco or may be rolled and cut. Bake in a hot oven from twelve to fifteen minutes.

Pineapple Drink

Canned pineapple juice, iced, with 3 tablespoons of lactose and cane sugar added to taste. Serve in an ordinary tumbler.

Pineapple Ice

½ cup confectioner's sugar
3 cups water
3 cups pineapple juice

Dissolve the sugar in the water and add the pineapple juice. Pour into the freezer. Pack with ice and salt. When frozen, remove from the freezer. Pack in a mold. Pack again in salt and ice until ready to serve. (Commercially prepared pineapple sherbet should not be used. It usually contains lemon and egg-white.)

Brown Sugar Candy

1 cup brown sugar
¼ cup water
Pinch of salt

Mix sugar, water and salt and cook until it forms a soft ball when dropped in cold water. Remove from the fire and cool. Beat until creamy.

SUGGESTED MENUS FOR DIET 4

Breakfast: Stewed peaches, fresh peaches, prunes
Cereals (as allowed), with prune juice or syrup from canned peaches.
Whole wheat bread,[14] crackers [15] with substitute for butter

Lunch: Beef bouillon
Meat (as allowed)
Spaghetti (milk-free)
Carrots or onions
Fresh or stewed peaches, prunes
Pineapple ice, pineapple
Hard candy, brown sugar candy
Pineapple juice
Whole wheat bread, crackers, with substitute for butter

3:30 P. M.: Pineapple juice
Graham cracker

Supper: May be selected from the lists for breakfast and lunch. Abbott's or Winthrop's viosterol may be included if ordered

DIET 5 (WITHOUT MILK)

Fruit

Apple
Apricot
Grapefruit
Lemon
Peaches
Pears
Prunes
Plums

Beverage

Grapefruit drink
Lemonade

Cereal

All cereals
Rice
Rye
Tapioca

Fish

Mackerel
Halibut
Codfish

Meat

Any kind

Vegetable

Peas
Beans (all kinds)
Squash
Asparagus

Carrots
Corn
Lettuce
White potato
Sweet potato

Eggs

Allowed

Bread

Whole wheat bread (white bread strictly forbidden) [14]
Graham crackers (National Biscuit Company) [15]
Ry-Krisp (Ralston-Purina Company)
Rye bread

Butter Substitute

Salted Crisco

Fat

Olive oil
Mazola
Crisco

Miscellaneous

Spaghetti, milk-free (not macaroni or noodles)
Salt
Karo
Refined sugar
Brown sugar
Gelatin
Baking soda
Baking powder
Molasses
Olives
Cream of tartar
Jelly
Jam
Honey
Flour
Sugar
Maple syrup
Tapioca
Hard candy (soft candy not allowed)
Cod liver oil
Viosterol
Crisco
Mazola
Wesson Oil
Olive oil

1. No foods other than those specified can be used.
2. The foods allowed may be eaten in unlimited quantities.
3. Even a minute amount of food not permitted on the diet may, if eaten, nullify an otherwise successful trial and confuse the solution hopelessly.

RECIPES FOR DIET 5

Sponge Cake

1 cup pastry flour, sifted
¼ teaspoon salt
4 eggs, separated
1 cup sugar
4 teaspoons lemon juice

Sift flour and salt together. Beat egg yolks until thick and lemon-colored. Add sugar gradually, beating constantly. Add lemon juice and mix thoroughly. Fold in flour alternately with stiffly beaten egg-whites. Do not beat, but bake at once in a floured, ungreased loaf tin in a slow oven (325 F.) from forty to sixty minutes. The recipe makes one small loaf.

Gingerbread

½ cup Crisco
½ cup brown sugar
2 eggs, well beaten
1 cup molasses
2½ cups whole wheat flour
1 cup boiling water
1½ teaspoons baking soda
½ teaspoon salt
1½ teaspoons ginger
1 teaspoon cinnamon

Cream the shortening and sugar together. Add the well beaten eggs and molasses, and blend thoroughly. Sift the flour with the soda and salt. Soak the spices in boiling water. Add the flour to the molasses mixture alternately with the water in which spices were soaked. Pour into a greased pan about 9 inches (22.8 cm.) square and bake in a moderate oven (350 F.) from thirty to forty minutes. Serve with fruit juice.

Plain Omelet

2 eggs, separated
2 tablespoons hot water
Salt and pepper

Beat the egg yolks until thick and lemon-colored. Add water and seasoning to taste. Beat the egg-whites until stiff and dry. Fold the whites into the egg yolk mixture. Pour into a hot greased omelet pan or frying-pan and spread evenly. Cook over a low flame until omelet is golden brown on the underside. Then place in a moderate oven (350 F.) until the top is dry and firm. Loosen from the pan with spatula and turn out on a platter. Serve at once. This recipe makes one generous serving.

Lemon Gelatin

½ teaspoon gelatin
1½ tablespoons lemon juice
Pinch of salt
1 tablespoon cold water
1 tablespoon sugar
½ cup boiling water

Soak gelatin in cold water five minutes and dissolve in boiling water. Add the sugar and stir until dissolved, then add the salt and lemon juice. Pour into a mold, first dipped in cold water and chill.

Lemon Ice

½ cup confectioner's sugar
3 cups lemon juice
3 cups water

Dissolve the sugar in water and add the lemon juice. Pour into a freezer packed with ice and salt. When frozen, remove from freezer and pack in a mold. Pack again in salt and ice until ready to serve. (Commercially made lemon ice may be used.)

Indian Pudding

2 tablespoons corn-meal
1 cup water
1 tablespoon sugar
1 tablespoon molasses
¼ teaspoon salt
¼ cup prunes, if desired

Cook the corn-meal and water in a double boiler twenty minutes. Add molasses, salt, sugar and prunes. Pour into a baking pan which has been greased with Mazola oil. Set in a pan of water and bake forty minutes in a slow oven. Serve with Karo.

Grapefruit Gelatin

1 tablespoon gelatin
¼ cup cold water
½ cup boiling water
1 cup grapefruit juice
¼ cup sugar
Pinch of salt

Soak gelatin in cold water five minutes and dissolve in boiling water. Add sugar and stir until dissolved, then add salt and grapefruit juice. Pour into a mold first dipped in cold water and chill.

Plum Gelatin

1 teaspoon gelatin
2 tablespoons cold water
¼ cup boiling water
¾ cup canned plum juice
Pinch of salt

Follow instructions for making grapefruit gelatin.

Grapefruit Drink

6 tablespoons (3 ounces) Karo
or
6 tablespoons powdered dextrose
3 ounces grapefruit juice (about ½ grapefruit)
Ice
Dash of salt

Heat the Karo slightly so that it will not be quite so thick; if dextrose is used mix with a little water and heat until dissolved. Add the grapefruit juice and ice. This drink will furnish 400 calories.

Apple Tapioca

¾ cup pearl tapioca
or
½ cup granulated tapioca
Cold water
2½ cups boiling water
½ teaspoon salt
7 sour apples
½ cup sugar

Soak the tapioca one hour in cold water. Drain, add boiling water and salt and cook in a double boiler until transparent. Core and pare the apples, arrange in a buttered pudding dish, fill the cavities with sugar, pour in the tapioca, and bake in moderate oven until the apples are soft. Granulated tapioca requires no soaking.

SUGGESTED MENUS FOR DIET 5

Breakfast: Baked apple, apple sauce, grapefruit, fresh or stewed peaches or pears
Any cereal, with molasses, maple syrup, juice from stewed apricots, or syrup from canned peaches
Soft boiled or poached egg on toasted whole wheat bread, plain omelet
Uneeda Biscuits, graham crackers, Ry-Krisp with salted Crisco or salted yellow petrolatum (butter strictly forbidden)
Whole wheat bread (as specified), rye bread
Grapefruit drink, lemonade
Bacon

Lunch: Meat
Mackerel, codfish, halibut
Peas, beans, carrots, corn, lettuce, squash, asparagus, white potato, sweet potato, rice
Uneeda Biscuits, graham crackers, Ry-Krisp with Crisco or salted yellow petrolatum, whole wheat bread (as specified), rye bread
Grapefruit drink, lemonade
Special sponge cake or gingerbread
Lemon gelatin, lemon ice
Fruits (as allowed)

Supper: May be selected from lists suggested for breakfast and lunch according to the age of the child

DIET 6 (WITHOUT WHEAT)

Fruit

Grapefruit	Apple
Lemon	Prunes
Peaches	Apricots
Pears	Bananas

Beverage

Milk	Lemonade
Grapefruit juice	Cream

Cereal

Rice	Post Toasties
Rye	Barley
Puffed Rice	Corn flakes
Rice Krispies	Oatmeal
Corn-meal	

Fish

Any kind

Meat

Any except prepared meats (hamburger, meat loaf, sausages), as they frequently contain wheat products as fillers

Vegetable

Carrots	Lettuce
Peas	Cauliflower
Beans	Onion
Squash	Celery
Asparagus	White potato

Eggs

Allowed

Bread

Corn pone	Barley and oatmeal muffins
Corn crisp	Rice and corn-meal muffins
Ry-Krisp	Rye-rice bread
Rye	100 per cent whole rye bread [13]
Rice muffins	

Fat

Any fat

Cheese

Cream cheese	Cottage cheese

Flour Substitutes

Rice flour	Barley flour
Rye flour	Corn-starch

Desserts

Bavarian cream
Corn-starch pudding
Fruit gelatin (of allowed fruits)
Tapioca pudding
Indian pudding
Brown betty
Simmons' arrowroot dessert (arrowroot, cane sugar, gelatin, vanillin, salt, coloring matter)
Ice cream
Sherbet

Miscellaneous

Viosterol
Sugar
Baking powder
Salt
Gelatin
Karo
Ice cream and sherbet
Potato chips
Tapioca
Green peppers
Vegetable shortening
Parsley
Pepper
Cream of tartar
Corn-starch
Olives (green, ripe or stuffed)
Baking soda
Molasses
Maple syrup
Hard candy, flavored with peppermint, wintergreen, lemon or cinnamon

1. No foods other than those specified can be used. Thus, gravy for the beef may be thickened only with rye flour or rice flour.

2. Even a minute amount of food not included in the diet may, if eaten, nullify an otherwise successful trial and confuse the solution.

RECIPES FOR DIET 6

Gravy

2 tablespoons rye flour
1 tablespoon fat
1 cup meat stock or water
Salt and pepper

Put Ry-Krisp wafers through a food-chopper, then roll fine with a rolling-pin. About 3 wafers will be needed to make 2 tablespoons of flour. Blend the shortening in which meat was cooked, or other shortening, with rye flour. Add the meat stock slowly and stir until thick. Season with salt and pepper. This makes 1 cup of gravy.

(An equal quantity of rye flour may be substituted for ordinary flour in thickening soups and sauces.)

Candied Apple Betty

2 large tart apples
¾ cup brown sugar
½ cup Ry-Krisp crumbs
¼ cup vegetable shortening

Pare the apples and slice thin. Cream the shortening and sugar thoroughly and add Ry-Krisp crumbs. Arrange alternate layers of sliced apple and Ry-Krisp mixture in a greased baking dish, having apples on the bottom and the sugar mixture on top. Bake in a moderate oven (325 F.) about one-half hour. The recipe makes a serving for three. (Canned or fresh sliced peaches may be substituted for the apples.)

Meat or Poultry Stuffing

2 dozen Ry-Krisp wafers
¾ cup hot meat stock or water
¼ cup vegetable shortening
1 green pepper, chopped
¼ cup chopped celery
2 tablespoons chopped parsley
Sage and pepper to taste

Put Ry-Krisp wafers through a food-chopper, then soak in hot stock. Add the remaining ingredients and mix well. This is sufficient for stuffing a 3 pound (1.3 Kg.) fowl.

Rye and Rice Muffins

⅓ cup rye flour
⅔ cup rice flour
½ level teaspoon baking soda
¾ level teaspoon cream of tartar
2 teaspoons sugar
⅓ teaspoon salt
⅔ cup milk
1 tablespoon butter

Sift the dry ingredients together. Add the milk and melted butter and beat thoroughly. Pour into muffin tins greased with butter or vegetable shortening and bake in a hot oven (400 F.) twenty-five minutes. The recipe makes 6 muffins, 2 inches (5 cm.) in diameter

Rye-Rice Bread

1⅓ cups rye flour
⅔ cup rice flour
½ teaspoon salt
6 teaspoons sugar
10 teaspoons baking powder
1⅓ cups water
2 teaspoons olive oil

Sift the dry ingredients together. Add water and oil, beating thoroughly. Pour into a loaf pan greased with olive oil and bake in a moderate oven (350 F.) forty minutes. The recipe makes 1 loaf.

Rice and Corn Meal Muffins

1⅓ cups rice flour
⅔ cup corn meal
½ cup sugar
½ teaspoon salt
10 teaspoons baking powder
1 cup water
¼ cup olive oil

Sift the dry ingredients together. Add water and oil and beat three minutes. Pour into muffin tins greased with olive oil and bake immediately in a moderate oven (350 F.) thirty minutes. The recipe makes 1 dozen muffins, 2 inches in diameter.

Corn Pone

¼ cup corn-meal
⅓ teaspoon salt
½ cup boiling water

Sift the corn-meal and salt together. Add boiling water to make a firm mixture. Shape into thin cakes, place in a pan well greased with bacon fat and bake in a hot oven (400 F.) from fifteen to twenty minutes. Makes 4 small cakes.

Barley Oatmeal Muffins

⅔ cup oatmeal
⅓ cup barley flour
1 tablespoon sugar
⅓ teaspoon salt
½ teaspoon baking soda
¾ teaspoon cream of tartar
⅓ cup water
1 tablespoon Wesson Oil

Mix in order given. Pour in muffin pans which have been greased with Wesson Oil. Bake in a hot oven from fifteen to twenty minutes. If the muffins are not eaten when fresh it is best to moisten them with a little water and reheat in the oven before serving.

Corn Crisps

½ cup corn-meal
½ teaspoon salt
½ cup boiling water

Add salt to corn-meal, add the boiling water and mix thoroughly. Shape the dough with the fingers, making oval pones ½ inch (1.2 cm.) thick. Place on a baking sheet which has been greased with butter and bake in a hot oven.

Apricot Gelatin

1 teaspoon gelatin
2 tablespoons cold water
¼ cup boiling water
¾ cup apricot juice
Pinch of salt
¼ cup sugar

Soak the gelatin in cold water five minutes and dissolve in boiling water. Add sugar and stir until dissolved, then add salt and apricot juice. Pour in a mold first dipped in cold water and chill.

Grapefruit Gelatin

1 tablespoon gelatin
¼ cup cold water
¼ cup sugar
½ cup boiling water
1 cup grapefruit juice
Pinch of salt

Soak the gelatin in cold water five minutes, then dissolve in boiling water. Add sugar and stir until dissolved, then add salt and grapefruit juice. Pour into a mold first dipped in cold water and chill.

Plum Gelatin

1 teaspoon gelatin
¾ cup canned plum juice
Pinch salt
2 tablespoons cold water
¼ cup boiling water

Follow directions for making grapefruit gelatin.

FOODS TO BE AVOIDED WITH DIET 6

Wheat Breads

Muffins
Popovers
Baking powder biscuits
Corn bread (unless made at home without wheat flour)
Crackers
Gluten bread
Graham bread
Pretzels
Rye bread (unless made at home with rye flour, or 100 per cent whole rye bread) [13]
White bread
Whole wheat bread
Zweiback

Cereal

All dry or cooked cereals made from or containing whole wheat, farina or bran

Flour

Wheat
Whole wheat
Graham
White
Any mixture of grain flours containing wheat

Miscellaneous

Gravy and cream sauce made of wheat products
Malt products
Yeast cakes

Pastry and Other Desserts

- Doughnuts
- Cakes
- Pies
- Cookies (unless made with wheat-free flours)

Wheat Products

- Bread crumbs
- Buckwheat
- Cracker crumbs
- Cracker meal
- Macaroni, noodles and spaghetti
- Vermicelli
- White flour
- Whole wheat flour
- Toast
- Graham flour

Care must be taken not to use any of the wheat products to thicken sauces, gravies or other foods, nor should flour or bread crumbs be used to retain the juices of meat about to be cooked. In short, it should be ascertained whether there is a possibility of the presence of a wheat product anywhere in the food, as the most minute amounts are troublesome.

SUGGESTED MENUS FOR DIET 6

Breakfast: Puffed Rice, Rice Krispies, corn-meal, Post Toasties, corn flakes or oatmeal with milk or cream
Fruit (those specified)
Milk
Corn pone, corn crisps, Ry-Krisps, rye-rice muffins, barley oatmeal muffins, rice and corn-meal muffins
Rye-rice bread, with butter, maple syrup, or molasses, 100 per cent whole rye bread [13]
Eggs (without toast, unless made from breads specified)

Lunch: Meat (specified), gravy, stuffing
Fish
Breads (specified)
Butter
Rice, potato
Vegetables (specified)
Milk
Cream cheese, cottage cheese
Bavarian cream, corn-starch pudding, fruit gelatin (of allowed fruits)
Tapioca pudding, Indian pudding, brown betty, Simmons' arrowroot dessert
Olives
Hard candy
Salads (plain or fruit)
Fruits (specified)

Supper: May be selected from the lists for breakfast and lunch, according to the age of the patient

DIET 7 (WITHOUT EGG)

Fruit

All kinds

Beverage

- Milk
- Lemonade

Cereal

All kinds

Fish

All kinds

Meat

All kinds except chicken and other fowl

Vegetable

All kinds

Eggs

Not allowed

Bread

Ry-Krisp
Whole wheat bread
Uneeda biscuits
Graham crackers
Rye bread
Rye and rice muffins
Rye-rice bread
Rice and corn-meal muffins
Corn pone
White bread

Starch

Spaghetti (macaroni and noodles prohibited)
Rice
Potato

Fat

Any fat
Butter

Cheese

Cottage
Cream

Desserts

Ice
Ice cream sherbet (if made at home without eggs)
Candied apple betty
Ry-Krisp pastry with fruit or jam

Miscellaneous

Royal, Snow King or any other baking powder which according to the label on the can does not contain egg
Flour (any kind)
Corn-starch
Sugar
Salt
Gelatin
Hard candy flavored with peppermint, wintergreen, lemon or cinnamon
Olives (ripe, green or stuffed)
Baking soda
Molasses
Maple syrup
Simmons' arrowroot dessert (arrowroot, cane sugar, gelatin, vanillin, salt and coloring matter)
Karo
Potato chips
Tapioca
Vegetable shortening

1. No foods other than those specified can be used.

2. There is no limit to the amount eaten of foods allowed.

3. Even a minute amount of food not included in the diet may, if eaten, nullify an otherwise successful trial and confuse the solution.

RECIPES FOR DIET 7

Rye and Rice Muffins

⅓ cup rye flour
⅔ cup rice flour
½ level teaspoon baking soda
¾ level teaspoon cream of tartar
2 teaspoons sugar
⅓ teaspoon salt
⅔ cup milk
1 tablespoon butter

Sift the dry ingredients together. Add the milk and melted butter and beat thoroughly. Pour into muffin tins greased with butter or vegetable shortening and bake in a hot oven (400 F.) twenty-five minutes. The recipe makes six muffins, 2 inches in diameter.

Rye-Rice Bread

1⅓ cups rye flour
⅔ cup rice flour
½ teaspoon salt
6 teaspoons sugar
10 teaspoons baking powder
1⅓ cups water
2 teaspoons olive oil

Sift the dry ingredients together. Add water and oil and beat thoroughly. Pour into a loaf pan greased with olive oil and bake in a moderate oven (350 F.) forty minutes. The recipe makes one loaf.

Rice and Corn Meal Muffins

1⅓ cups rice flour
⅔ cup corn-meal
½ cup sugar
½ teaspoon salt
10 teaspoons baking powder
1 cup water
¼ cup olive oil

Sift the dry ingredients together. Add water and oil and beat three minutes. Pour into muffin tins greased with olive oil and bake immediately in a moderate oven (350 F.). The recipe makes one dozen muffins, 2 inches in diameter.

Corn Pone

¼ cup corn-meal
⅓ teaspoon salt
½ cup boiling water

Sift the corn-meal and salt together. Add boiling water to make a firm mixture. Shape into thin cakes, place in a pan well greased with bacon fat and bake in a hot oven (400 F.) from fifteen to twenty minutes. The recipe makes four small cakes.

Candied Apple Betty

2 large tart apples
¾ cup brown sugar
½ cup Ry-Krisp crumbs
¼ cup vegetable shortening

Pare the apples and slice thin. Cream the shortening and sugar thoroughly and add Ry-Krisp crumbs. Arrange alternate layers of sliced apples and the Ry-Krisp mixture in a greased baking dish having apples on the bottom and the sugar mixture on top. Bake in a moderate oven (325 F.) about one-half hour. The recipe makes a serving for three. (Canned or fresh sliced peaches may be substituted for apples.)

FOODS TO BE AVOIDED WITH DIET 7

Egg Dishes and Recipes

Baking powder (other than Royal, Snow King or any other not containing egg)
Boiled dressings
Breaded foods (in which the adherent used is an egg mixture)
Custards

Doughnuts
Dried eggs
Dumplings
Egg drinks
Egg sauce
Egg chips
Fritters
Frosting (unless home-made without eggs)
Griddle cakes
Ice cream (unless home-made without eggs)
Macaroni
Macaroons
Malted cocoa drinks
Marshmallows
Mayonnaise
Meringue
Noodles
Ovaltine
Pretzels
Puddings (unless made without eggs)
Spanish cream
Timbales
Waffles

This list points out foods most likely to be used. Eggs should not be used in any way, either as such or as an ingredient in a prepared food. An egg should not be used to clear soup. The utmost caution should be used in purchasing foods which are prepared, to be sure that there is no egg content.

SUMMARY

General indications for elimination diets for children have been discussed.

The selection of the appropriate trial diet has been outlined.

A series of seven type diets for children has been presented in detail.

215 East Seventy-Second Street.

Pediatric Biographies

COSTE AND GIOJA

1838?

A NOTE ON THE HISTORY OF PSEUDOHYPERTROPHIC MUSCULAR DYSTROPHY

JOHN RUHRÄH, M.D.
BALTIMORE

The history of pseudohypertrophic muscular dystrophy is usually said to date from Duchenne of Boulogne, who gave the first extended account of it, but it had been noted before by others, although it is doubtful whether Duchenne knew of these. Probably there are references to the condition in the earlier literature, but the earliest one known to me is that by Coste and Gioja which appeared in the *Annali clinici dello ospedale degl' incurabili di Napoli,* in 1838 and which was noted in *Schmidt's Jahrbücher der in- und ausländischen gesammten Medizin.*[1] One would doubtless have to go to Italy to find out anything concerning Coste and Gioja. Castiglione did not mention them, nor did any of the other writers on medical biography whose books have been consulted. The cases which Coste and Gioja reported are so typical and so striking that the authors deserve a note and a place in the list of those who have helped to make pediatrics by describing hitherto unknown or unreported diseases.

Another report is that by William John Little (1810-1894), whose name is associated with congenital spastic diplegia and who just missed describing poliomyelitis in his book on "Clubfoot." In his book entitled "On the Nature and Treatment of the Deformities of the Human Frame," published in 1853, he gave an account of two cases occurring in brothers aged 12 and 14. He noted what he termed "adipose degeneration" of the muscles and gave a remarkable account of the symptoms and course of the disease.

Coste and Gioja's report is as follows:

> Two brothers, born in the country, were well and strong until ten years of age. About this time they went to a very damp and cold village, where they worked on a farm. Their health was soon affected; the muscles of the lower extremities increased in size; the whole muscular system became involved and

1. Coste and Gioja, cited in Schmidt's Jahrb. **24**:176, 1839.

both brothers became unfitted for labor so they were sent to the city where they entered the surgical clinic. They used the baths of Ischia, but their condition became continually worse. The increase in the size of the muscle system was extraordinary; one of them died with symptoms of hypertrophy of the heart (an autopsy could not be made) and the other remained in the hospital for incurables. He is 18 years old and in the following condition: He is small and through the absence of the signs of puberty resembles a 10-12 year old child. The dimension of his head in relation to the size of his body is nevertheless very considerable. The tongue is at least a third larger than in the natural condition; it fills the mouth and hinders chewing, speaking and swallowing. The muscles of mastication are very voluminous; the breast short; the ribs are thin. The abdomen, in consequence of the thickness and stiffness of its muscles, especially through the bulging of the rectus, is large and hard. The muscles of the head and neck do not show anything unusual; of the back muscles the upper part of the trapezius shows a marked hypertrophy, and the digitations of the latissimus dorsi, the quadrati lumborum are twice their natural size, but the most marked changes are noted in the upper and lower limbs. The deltoids are three times as large as ordinary, the gastrocnemii make an extraordinary bulge, and the tendons of these muscles are thin and hard. The remaining muscles are relatively nearly as hypertrophied as those just described. The bones of the extremities appear thin and as if atrophied, especially on the condyles of the hip and shin bone. The forearm and the fingers remain passive in flexion, and the patient can neither extend nor use them. The hip is likewise flexed on the pelvis and the lower leg in the hip, the heels touching the buttocks. The feet are crooked so that their backs are in line with the outer ankle and the soles in the direction of the inner ankle. The skin covering the hypertrophied muscles is dark red and shows varicose veins. The functions of the generative organs are scarcely developed. The other functions are normal. The patient uses iodine internally and externally indeed with some benefit.

Pediatrics in Art

MUSCULAR HYPERTROPHY

JOHN RUHRÄH, M.D.
BALTIMORE

Although pseudohypertrophic muscular dystrophy apparently is not considered in the medical literature until 1838, it seems possible that a patient with the disease may have served as a suggestion for a group of young dancers seen in the illustration. Of course some artists liked

"The Dance of Love," showing muscular hypertrophy.

to portray exaggerated muscular development, but this was usually in connection with older persons.

Artists of all ages have delighted in portraying fat, well nourished children, so examples of obesity are common enough. There is in the Musées des Antiquités, in Istanbul, a small piece showing two Greek boys quarreling over cocks which look as if they might have been fighting. The boys are obese, but they also show unusually well developed muscles.

The picture shown here is on a plate in the Royal Gallery in Modena. It is done after the manner of Raphael by some unknown artist working in the potteries of Urbino. The title of the picture is "The Dance of Love."

Abstracts from Current Literature

Pathology, Bacteriology and Biochemistry

THE EFFECT OF SINGLE AND MULTIPLE DOSES OF THE PARATHYROID HORMONE ON THE CALCIFICATION OF THE DENTIN OF THE RAT INCISOR. I. SCHOUR, W. R. TWEEDY and F. A. MCJUNKIN, Am. J. Path. **10**:321 (May) 1934.

The effect of single and multiple injections of parathyroid hormone on the incisor of the white rat in respect to microscopic alterations and blood calcium changes was studied in twenty-nine animals and seven controls. The histologic observations were: 1. Hypoplasia of the enamel began immediately after the first injection in five of the animals. 2. The alveolar bone showed an abnormal increase in osteoclasts in fourteen rats and a fibrous change of the bone marrow in three of the rats that were given three or more injections of the parathyroid hormone. 3. The principal changes were observed in the calcification of the dentin. The experimental animals showed a primary hypocalcified stripe in the dentin that was being calcified during the immediate effect of the first injection and a secondary hypercalcified stripe in the dentin that was being calcified subsequently. The extent of and the variations within the secondary stripe varied with the number and units of the hormone preparations injected and also with the duration of the experiment.

It is believed that the experimental pattern in the dentin represents its response to the changes in the calcium and phosphorous metabolism induced by the injections of the parathyroid hormone. The dentin reaction can be explained best by the theory that the parathyroid hormone controls a fraction of the serum calcium.

AUTHOR'S SUMMARY (MOORE, N. Y.)

THE PHYSIOLOGIC MAINTENANCE OF THE MALE SEX GLANDS: THE EFFECT OF ANDROTIN ON HYPOPHYSECTOMIZED RATS. EUGENE L. WALSH, W. KENNETH CUYLER and D. ROY MCCULLAGH, Am. J. Physiol. **107**:508 (Feb.) 1934.

The male sex hormone from urine prevented atrophy of the sex glands in hypophysectomized rats.

NOURSE, Cleveland.

STUDIES ON THE RELATION OF THE ADRENAL GLANDS TO ALLERGIC PHENOMENA: I. THE OUTPUT OF EPINEPHRINE DURING ANAPHYLACTIC SHOCK IN DOGS. MILTON B. COHEN, J. A. RUDOLPH, P. WASSERMAN and J. M. ROGOFF, J. Allergy **5**:221 (March) 1934.

Experiments were done on nine dogs to determine whether or not the epinephrine output of the adrenal medulla was altered during anaphylactic shock. The animals were sensitized to horse serum. The shock experiments were done from four to five weeks later. Two of the dogs failed to show symptoms of shock when horse serum was injected intravenously. In the shocked animals there were a decided drop in blood pressure and delayed clotting of the blood. The rate of flow of the blood through the adrenals was greatly reduced. There was no significant alteration in the rate of secretion of epinephrine from the adrenal gland.

HOYER, Cincinnati.

STUDIES OF THE ANAPHYLACTIC ANTIBODY: I, II AND III. OSCAR SWINEFORD JR., J. Allergy **5**:265 (March) 1934.

The studies described were an endeavor to show that the anaphylactic antibody can be refined; that it is widely distributed through the globular fractions, and that it protects guinea-pigs against shocking doses of horse serum.

The experiments showed that guinea-pigs can be passively sensitized to a solution of antibody; the anaphylactic antibody is present in both the water-soluble

and the water-insoluble globulin fraction of immune serum. Sensitized guinea-pigs were appreciably protected from shocking doses of horse serum by the water-soluble solution of antibody and completely protected by specific water-insoluble antibody factors.

HOYER, Cincinnati.

OVARIES AND TESTICLES OF THE FETUS OF THE HORSE AS A SOURCE OF HORMONES. J. BRILL, Compt. rend. Soc. de biol. **113**:951 (June 24) 1933.

The origin of the enormous quantities of an estrogenic substance found in the gravid mare (100,000 units per liter of urine) is not sufficiently proved. Some believe that it originates from the maternal ovaries; others, from the placenta. Brill noticed the considerable growth of the ovaries and the testicles of the fetuses at different periods during gestation in the horse. He noted that the maternal ovaries go through a period of decline during the latter part of pregnancy. The fetal ovaries increase in size, as is shown by the fact that he was able to obtain 1 unit of estrogenic hormone to each 0.2 Gm. of fetal ovarian pulp.

The fetal ovary is therefore one of the origins of the hormone. A statement is made that the testicular hormone parallels the ovarian.

WAHL, Cleveland.

VARIATIONS IN BLOOD CALCIUM FRACTIONS FOLLOWING ADMINISTRATION OF EPINEPHRINE. C. ROSSO, Clin. pediat. **16**:229 (March) 1934.

The intravenous administration of epinephrine hydrochloride in dogs causes transformation of colloidal calcium into ultrafiltrable calcium.

DOOLEY, New York.

EXPERIMENTAL CHRONIC CARBON MONOXIDE POISONING. H. FETZER and P. G. WEILAND, Arch. f. Hyg. **112**:95 (May) 1934.

Fetzer and Weiland used illuminating gas containing 19.5 per cent carbon monoxide in their experiments on dogs and guinea-pigs for the reason that this is the most common source of chronic carbon monoxide poisoning in man. The average concentration of carbon monoxide in the room in which the animals were kept was 0.1 per cent. This concentration was borne by the animals without any signs of acute poisoning. The guinea-pigs lived in this atmosphere for four hours a day for four months. Six dogs were used, four being exposed daily for from three to four hours for three months, while two dogs were kept as controls. The conditions of the experiment were carefully controlled as to adequate diet and cleanliness of the experimental room.

The principal observations were falling out of the hair, salivation and transient disturbances of body temperature and gait. In dogs there was a slight increase in the amount of hemoglobin and a slight decrease in the resistance of the red blood cells. Immunity to disease did not seem to be influenced. The resistance of guinea-pigs to inoculation against tuberculosis was not significantly affected. Disturbances of the carbohydrate metabolism could not be demonstrated in either type of animal. There was no appreciable influence on the alkali reserve.

Fetzer and Weiland believe from their own experience and from reports in the literature that all the symptoms of chronic carbon monoxide poisoning can be explained on the basis that the primary toxic effect of the gas is on the central nervous system.

GLASER, Rochester, N. Y.

DEPENDENCE OF THE RESULTS OF THE FUNCTIONAL TEST BY WATER LOADING ACCORDING TO FOLGARD ON THE STATE OF THE THYROID FUNCTION. V. T. BOYEFF, Vrach. delo **17**:431, 1934.

1. In decreased function of the thyroid gland the water test of Folgard results in a retardation of the excretion of water (to from five to eleven hours) or in a remarkably slow excretion. There is an increase of the water stores of the

body; the quantity of urine is markedly increased, and the urine has a low concentration. Treatment with thyroid substances is able to be helpful in improving this state.

2. In increased function of the thyroid gland the reaction to the water test is mostly accelerated (1,500 cc. is eliminated within from two and a half to three hours), as is the resorption of physiologic solution of sodium chloride (within from forty to fifty-five minutes). The concentration test gives normal results.

3. The water test, as well as the test with physiologic solution of sodium chloride, are good diagnostic methods for determining disturbances of the thyroid function and intermediate water metabolism.

4. As the observations have shown, changes in the thyroid function can be a serious impediment to the correct evaluation of the results of the test of the water-excreting function of the kidneys and the concentration capacity of the latter. These tests have no practical value in the diagnosis of kidney disease, as they are able to provoke great changes in consequence of the altered function of the thyroid gland.

YAMPOLSKY, Atlanta, Ga.

Nutrition

NATURAL AND INDUCED VARIATIONS IN THE VITAMIN VALUES OF MILK. H. C. SHERMAN, Am. J. Pub. Health **23**:1031 (Oct.) 1933.

Sherman summarizes the present knowledge of the vitamin values of dairy milk produced with modern feeding and states that cow's milk contains a liberal and practically constant supply of vitamin A as well as of vitamin B. There is a relatively low concentration of vitamin C, but large amounts of milk consumed make it an important source of this vitamin. The vitamin D content of milk is low and, especially in northern latitudes, it would be advantageous to enrich the milk by direct additions of a vitamin D concentrate, irradiation of the milk, feeding of irradiated yeast or other suitable irradiated material to the cow or irradiation of the cow. There is considerable evidence that cow's milk is a rich and constant source of vitamin G (B_2).

MCBRYDE, Durham, N. C.

THE CONTROL OF CARBOHYDRATE METABOLISM. J. J. K. MACLEOD, Bull. Johns Hopkins Hosp. **54**:79 (Feb.) 1934.

LECTURE 1.—In the diabetic animal, insulin lowers the blood sugar level, and when carbohydrate food is given the liver, which was previously depleted, becomes loaded with glycogen, and the respiratory quotient is raised. These results must be due partly to the conversion of dextrose into glycogen and partly to an increase in oxidation in the tissues. Insulin lowers the blood sugar level in the normal animal, but an increase in glycogen is not produced in the rabbit which has previously fasted. In rabbits fed starchy foods, the glycogen of the liver is greatly reduced, while the muscles may become free from glycogen. Ten years of active research have not produced any very clear idea of how insulin affects glycogen formation. Similar confusion exists with regard to the influence of insulin on the respiratory exchange. A critical appraisal of balance experiments in the eviscerated preparation follows, which is extremely valuable in pointing out the possible sources of error in such investigations. Experimental evidence is given bearing on the interpretation of respiratory quotients and the question of pure carbohydrate muscle metabolism or the utilization of all three foodstuffs during muscular activity.

LECTURE 2.—The first part of this section is devoted to the conditions apart from insulin activity which affect glycogen formation. In experimental work one must control conditions in regard to the species, age, previous diet, duration of the fast, condition of the ductless glands, season of the year, cyclic changes, anesthesia, blood pressure, anoxemia, stunning and postmortem changes.

The influence of insulin on glycogen metabolism is then discussed. Evidence offered by three series of experiments leads only to the conclusion that an excess

of insulin in the presence of a high concentration of dextrose in the blood leads to glycogen formation in the muscles, but such a process cannot be responsible for the initial fall in the blood sugar level. There is no decided and constant increase in the respiratory quotient and oxygen consumption during the fall in the blood sugar level. Increased combustion cannot be the primary cause of the disappearance of sugar.

Epinephrine given in such small doses that its other measurable effects are not detectable causes a rise in the blood sugar level, a comparable rise in the blood lactic acid content, a fall in the glycogen in the muscles and a rise in the glycogen in the liver. The possible balance relationship between epinephrine and insulin is discussed.

The nerve control of the secretion of insulin is supported by some work, but there is no substantial evidence that the secretion of insulin is regulated by a nerve mechanism.

LECTURE 3.—The puncture experiments of Claude Bernard are outlined. Similar experiments on animals under amytal or phenobarbital anesthesia failed to produce the hyperglycemia which constantly follows when a local anesthetic is given. Experiments in decerebration led to the conclusion that in the pons there is a diabetogenic center having a profound influence on the blood sugar level. Further work seemed to show that the mechanism of sugar production controlled by the vagus is a process of glyconeogenesis, whereas the sympathetic action depends on glycogenolysis. The parasympathetic pathway stimulates the secretion of sugar by the liver, but this may be blocked by section of the vagi, atropine or amytal. Impulses through the splanchnic nerves producing glycogenolysis by direct action on the liver and possibly through stimulation of the adrenals, may be blocked by cutting the splanchnic nerves, by adrenalectomy or by ergotamine.

Is the increase in blood sugar due to the addition of dextrose or to slower removal from the blood stream? The usual conception of sugar being poured in as a result of glycogenolysis is difficult to correlate with the increases in blood sugar when the liver stores are practically nonexistent. The conversion of lactic acid derived from muscle glycogen into sufficient dextrose by the liver to produce the hyperglycemia is not supported by the evidence available. Glyconeogenesis cannot be ruled out, but evidence is lacking. The possibility that the rate of migration of sugar into the tissues is interfered with awaits further investigation. There is some evidence that phlorhizin lowers the threshold of other tissues than those of the kidney to dextrose. Piqûre has no effect in phlorhizin poisoning unless both kidneys are tied off, when the usual hyperglycemic response occurs.

BRUSH, New York.

EFFECTS OF COD-LIVER OIL ON BASAL METABOLISM AND ON THE THYROID GLAND. T. C. SHERWOOD, L. A. TOTH and K. CARR, Endocrinology **18**:254 (March-April) 1934.

The authors cite a few of the "numerous experiments which have shown that therapeutic doses of cod liver oil cause toxic effects and organic changes of a regressive type." Agduhr demonstrated that cats and dogs showed no sign of heat when doses of 1 to 5 cc. of cod liver oil per kilogram of body weight per day were added to the basal diet, beginning at the age of 1 month and continuing for one year. The number of red blood corpuscles was reduced; the spleen was abundantly supplied with blood pigments, indicating increased destruction of blood cells, and regressive changes were noted in various organs. The weight curves of mice similarly treated showed disturbing alterations. Slagswold noted poisoning among cattle by cod liver oil. Norris and Church expressed the belief that toxic effects from some cod liver oils were due to iso-amylamine. Harris and Moore noted retardation of growth rates when vitamin A and D concentrates were given. Riddle and Baucher demonstrated that high metabolism in pigeons was accompanied by a higher hemoglobin and erythrocyte value, the opposite effect being found with low metabolism.

In view of these facts, the authors decided to study the effect of cod liver oil on the metabolism and thyroid glands of rats. Twenty-seven animals were given from 1 to 5 cc. of cod liver oil per kilogram of body weight per day, and of thirty animals used as controls ten received corn oil, ten viosterol and ten cod liver oil minus vitamin A. No change in the basal metabolic rate could be demonstrated, but a decided change was produced in the thyroid glands of the animals receiving cod liver oil, namely, depletion of the colloid content of the acini. In the three control groups the thyroid was not affected.

JACOBSEN, Buffalo.

STUDIES ON THE LEUCOCYTE CONTENT OF MILK DRAWN FROM BRUCELLA ABORTUS INFECTED UDDERS. C. C. PROUTY, J. Bact. **27**:293 (March) 1934.

A study was made of the leukocyte content of the milk from eighteen cows in relation to the presence of Brucella abortus within the udder. Thirteen cows were found by cultural methods to harbor Brucella abortus in one or more quarters of the udder. Twenty-one of the seventy-two quarters examined were found to be infected. The average leukocyte count per cubic centimeter of milk from the twenty-one infected quarters was 355,000, as compared with 343,000 for milk from the fifty-one quarters that gave negative cultural findings. Two of the quarters infected with Brucella abortus and two of the noninfected quarters produced milk of a high leukocyte count, owing to the presence of active streptococcic mastitis. When the samples of milk from these quarters were omitted in computing averages, average cell counts of 145,000 and 185,000 per cubic centimeter were obtained for the samples from the quarters infected with Brucella abortus and from the non-infected quarters, respectively. In spite of conclusions to the contrary in the literature, Prouty believes that his study so far shows that there is no significant difference in the leukocyte count of milk from the udders of cows infected with Brucella abortus and from those of animals free from this disease.

STOESSER, Minneapolis.

STUDIES OF PHOSPHORUS OF BLOOD: THE PARTITION OF PHOSPHORUS IN WHOLE BLOOD AND SERUM, THE SERUM CALCIUM AND PLASMA PHOSPHATASE FROM BIRTH TO MATURITY. GENEVIEVE STEARNS and EDNA WARWEG, J. Biol. Chem. **102**:749 (Oct.) 1933.

The inorganic, lipoid, ester and total phosphorus contents of whole blood and serum, together with the serum calcium and plasma phosphatase, are reported in a series of one hundred and fifty determinations on blood from one hundred and twenty-four children ranging in age from birth to maturity.

No component of phosphorus studied is constant throughout the entire period of growth. Each component appears to reach a maximum value at some time during infancy or early childhood. The age at which the maximum value is reached and the length of time it is maintained vary for each component.

The curve of corpuscular volume during the period of growth was determined. The percentage of corpuscles in the blood is high in the new-born, but drops rapidly during the first month. The average value rises slowly during infancy and very slowly during childhood. The value for adults is still somewhat lower than that at birth.

The serum calcium tends to be higher in the new-born than during later infancy. The level during infancy likewise tends to be higher than that during childhood. After the third year the values remain constant throughout childhood and early adult life.

The phosphatase of plasma is low at birth, but rises rapidly to a maximum during the first month of life and remains fairly high until during the second year. The values in later childhood are within the range of those for adults.

AUTHORS' SUMMARY.

THE DIURNAL RHYTHM IN WATER AND MINERAL EXCHANGE. ROBERT C. MANCHESTER, J. Clin. Investigation **12**:995 (Nov.) 1933.

In studies of two mildly epileptic children and one normal child there was found a diurnal rhythm in the mineral and water balance, which was characterized by a greater excretion of sodium, potassium and chloride and a greater volume of urine during the day than at night. A negative water balance, with a maximum volume of urine and a maximum output of urinary sodium, potassium and chloride, reached a maximum from 6:00 a. m. to 12:00 noon, whereas the water balance became positive, with a minimum volume of urine and a minimum excretion of sodium potassium and chloride from 12:00 midnight to 6:00 a. m. The mechanism maintaining this rhythm is thought to be dependent on differences between the sleeping and waking states rather than on changes in the degree of physical activity.

GUEST, Cincinnati.

ELECTROLYTES IN HUMAN TISSUE: III. A COMPARISON OF NORMAL HEARTS WITH HEARTS SHOWING CONGESTIVE HEART FAILURE. WALTER E. WILKINS and GLENN E. CULLEN, J. Clin. Investigation **12**:1063 (Nov.) 1933.

Analyses of the water content, phosphorus, sodium, potassium, magnesium and calcium in the right and left ventricles of seventeen human hearts (five normal, four from persons with cardiac disease who died of other causes and eight from persons who died with congestive heart failure) were made. The sums of the individual bases showed that the two ventricles did not differ essentially in their total base content. In both ventricles of the diseased hearts there was an increase of water and of sodium, whereas the phosphorus, potassium and magnesium were decreased. There were no consistent variations in the calcium content.

GUEST, Cincinnati.

BLOOD PLASMA PROTEIN REGENERATION CONTROLLED BY DIET: I. LIVER AND CASEIN AS POTENT DIET FACTORS. RUSSELL L. HOLMAN, EARLE B. MAHONEY and GEORGE H. WHIPPLE, J. Exper. Med. **59**:251 (March) 1934.

The authors have ample evidence to show that regeneration of the blood plasma protein in the dog can be modified at will by dietary factors. The evidence in this article indicates that feeding liver and casein is very potent in effecting rapid regeneration of the plasma protein. The authors are testing systematically other proteins.

The blood plasma proteins are reduced by plasmapheresis close to the level in edema (from 3.5 to 4 per cent) and are kept at this level by suitable exchanges almost daily. A basal ration is used that is poor in vegetable protein (potato) and contains no animal protein. On this ratio the nitrogen balance of the dog can be kept normal, but only about 2 Gm. of plasma protein per kilogram of body weight per week is produced. With the feeding of liver or casein this production can be increased threefold or fourfold.

A reversal of the albumin-globulin ratio may be observed in dogs fed the basal diet alone. The reversal always follows plasmapheresis with the dog on the basal diet, and the total plasma protein output consists approximately of 2 parts of globulin and 1 part of albumin. A liver diet raises the production and output of albumin and brings the ratio back toward normal.

Eventually all this information will be of interest and practical use to physicians who have patients showing hypoproteinemia or loss of blood protein. The maintenance of blood proteins above the level in edema has a practical bearing on the treatment of certain patients with nephrosis and nephritis.

KNICKERBOCKER, Dallas, Texas.

VITAMIN D CERTIFIED MILK. W. E. BROWN, J. Med. **15**:88 (April) 1934.

The antirachitic potency of vitamin D certified milk (Cincinnati) was determined from ten samples taken at random during January 1934. This month was chosen because of the small amount of available sunlight. At least 160 rat units (Steenbock) of vitamin D per quart were found for each sample of milk examined.

NELSON, Cincinnati.

INFANT NUTRITION: BACK TO FIRST PRINCIPLES. JESSE R. GERSTLEY, M. Clin. North America **17**:1607 (May) 1934.

In this article Gerstley reviews the results of his investigations during the past few years on carbohydrate metabolism. Studying the acidity of the stools of breast fed infants and those fed mixtures of cow's milk, he found that the degree of acidity as evidenced by the hydrogen ion concentration is never so great in the latter as in the former. Gram for gram, the stools of babies fed cow's milk contain less acid. The addition of lactose to dilutions of cow's milk often results in an increased production of acid, but this is so metabolized in the intestine that the degree of acidity never closely approaches that of the breast fed infant, even when diarrhea occurs. The diarrheas gave no indication of increased intensity of fermentation. These results with dilutions of milk led Gerstley to experiment with the addition of larger amounts of lactose to formulas of whole milk. When the lactose was increased to 12 per cent, the stools began to resemble in appearance, consistency, odor and acidity those of the breast fed infant. The additional lactose, plus the 4 per cent present in cow's milk, gives a relation of lactose to protein of 4:1, which is approximately that of mother's milk. It was also found that the addition of 12 per cent lactose to whole cow's milk was followed by a definite but not constant transformation of the gram-negative intestinal flora of the stools of infants fed cow's milk to the gram-positive flora of those of the breast fed infants. Further experience with the feeding of these high calorie mixtures showed that the initial rapid gain in weight was followed by a period during which the infant ceased to gain and became vulnerable to incidental infections to which it reacted violently. By diluting the mixture a more acceptable formula was obtained, on which the infant continued to thrive.

At this stage of his investigations Gerstley is not ready to draw definite conclusions as to their bearing on the baby as a whole. He believes, however, that the results obtained should dispose of the ideas generally held concerning the part played by carbohydrate fermentation in the diarrheas of infancy. Throughout this article he stresses the importance of the study of the infant as a whole rather than basing feeding and treatment on such symptoms as acidity, frequency and consistency of the stool.

EUGENE SMITH, Ogden, Utah.

THE MANAGEMENT OF BREAST-FEEDING IN GENERAL PRACTICE. H. R. YOUNGMAN, Brit. M. J. **1**:480 (March 17) 1934.

Youngman discusses the management of breast feeding, beginning with the antenatal care of the mother's breasts, and continues with a discussion of the physiology of the weight curve of the child, the training in regard to proper hours of nursing and tests of overfeeding and underfeeding by trial weighing. A table of symptoms due to overfeeding and underfeeding is included. All the practices described are based on Youngman's own experience.

ROYSTER, University, Va.

"LOW PROTEIN MILK" AS MEDICATED NOURISHMENT IN EARLY INFANCY. E. HURMUZACHE, Bull. Soc. de pédiat. de Iasi **4**:124 (Oct.-Dec.) 1933.

In eighteen infants with gastro-intestinal disorders or marasmus Hurmuzache obtained excellent results by the use of a special milk preparation. In preparing this formula 1 liter of milk is boiled, the cream skimmed off, 3 Gm. of calcium lactate added and the preparation filtered through a fine sieve. This milk then

contains from 17 to 20 Gm. of casein and from 29 to 40 Gm. of fat per liter. It is claimed that the calcium lactate reacts with hydrochloric acid in the stomach, producing lactic acid, which increases the beneficial action of the milk.

LeMaster, Evanston, Ill.

Hypothrepsia with Hyperglycemia in a Weak Offspring of a Drug Addict; Good Results of Treatment with Insulin. G. Blechmann, A. Chabanier and J. Pruneau, Bull. Soc. de pédiat. de Paris **31**:195 (April 25) 1933.

A drug addict, who had been taking morphine in large doses for years, gave birth to a girl weighing 2,600 Gm., prematurely born at eight months. The mother had periods of psychotic symptoms with suicidal ideas, marked anorexia and loss of weight during the entire pregnancy. The infant took feedings of condensed milk, and then ass' milk poorly and lost weight. When she was 15 days old she was given injections of insulin and dextrose-saline solution daily, with marked improvement in appetite and increase in weight. At the age of 2½ months the urine showed 3.54 Gm. of sugar per liter and no acetone. A week later there was no glycosuria, although the doses of insulin were not increased. The fasting blood sugar was 0.13 Gm. per hundred cubic centimeters. The sugar tolerance curve showed increased and prolonged hyperglycemia. At the end of the fifth month the infant began to have convulsions which had no relation to the injections of insulin. She was given a course of treatment with sulpharsphenamine. At 13 months the blood sugar was normal, after she had not been observed for more than five months. Toxic injury to the pancreas, with resultant hypo-insulinism, is mentioned as a possible explanation of the transient hyperglycemia.

Benjamin, Montreal, Canada.

A Fatal Case of Anaphylaxis to Mother's Milk in Infancy. J. Leveuf and H. Vignes, Bull. Soc. de pédiat. de Paris **31**:239 (May 16) 1933.

A new-born boy vomited a great deal and lost considerable weight for the first five days of life. Breast feeding was discontinued and he was given a formula made up with a dried milk preparation. He improved steadily and gained weight until the tenth day after birth, when he left the hospital with his mother. At her request breast milk feeding was again attempted. He began to vomit, became cyanosed and presented the picture characteristic of severe shock. He died a few hours later. Necropsy revealed no abnormality of the digestive tract. It is believed that death was due to anaphylaxis as a result of sensitization to the mother's milk.

Benjamin, Montreal, Conada.

Irradiated Sterols and the Ultraviolet Rays: Physiologic and Pathologic Differences. P. Duhem and E. Huaut, Bull. Soc. de pédiat. de Paris **31**:310 (July 11) 1933.

The effects produced on the vegetative nervous system by the administration of a preparation of pure viosterol and cholesterol were found to be insignificant as compared with changes obtained by means of exposure to the ultraviolet rays. Children of from 4 to 14 years of age with various pathologic conditions were given from 15 to 30 drops of the irradiated sterol preparation, as compared with from four to six minutes of exposure to the ultraviolet rays. The effect on the neurovegetative system was observed by the use of the oculocardiac reflex and by the action of epinephrine and of atropine on the heart beat, before each treatment and again ten minutes after. Invariably the results obtained after the ingestion of the irradiated sterol preparation were insignificant as compared with the marked changes obtained after exposure to the ultraviolet rays. The conclusion drawn is that the latter is the better therapeutic agent.

Benjamin, Montreal, Canada.

UTILIZATION OF A CALCIUM MILK IN THE DIET OF INFANTS. E. LESNÉ and G. DREYFUSS-SÉE, Bull. Soc. de pédiat. de Paris **31**:347 (July 11) 1933.

For the past three years the infants in the crèche of the Trousseau Hospital have been fed milk modified by the addition of calcium lactate. It is prepared by adding 3 Gm. of calcium lactate to a liter of boiling skimmed milk; the milk is then withdrawn from the fire, and after thirty seconds it is passed through a large fine strainer, this taking not more than thirty seconds. The milk is used undiluted, with sugar added. It may be diluted, as desired, with water, and the fat content may be increased, if desired, by using whole milk instead of skimmed milk. If too much calcium lactate is added or the milk is permitted to boil too long after the addition of the calcium lactate, the casein content is reduced too much, rendering the feeding inadequate. When prepared according to directions, the product contains about 17 to 18 Gm. of casein per liter (approximately the amount in breast milk) and the butter fat content is from 3 to 6 Gm. per liter. This preparation is particularly indicated for hypothreptic infants and for those with digestive disturbances as manifested by vomiting and diarrhea. Good results have been obtained by its use in infants with eczema. It also supplies a suitable diet for bridging the gap between breast milk and cow's milk in certain cases. Its advantages are that it is readily digestible, easily assimilable, has no acid taste and is therefore well taken by infants who object to acidified milk and is inexpensive and simple to prepare.

BENJAMIN, Montreal, Canada.

BASAL METABOLISM IN INFANTS. H. JANET and M. BOCHET, Bull. Soc. de pédiat. de Paris **31**:359 (July 11) 1933.

The basal metabolism of one hundred infants, some of whom were normal and others considered as abnormal, was studied by means of a respiratory sac devised by the authors. Determinations were made by recording the consumption of oxygen, the amount of carbon dioxide utilized and the respiratory quotient. The difficulty of obtaining readings for the infants under conditions of fasting and complete rest is obvious; the infants were observed as long as possible after feeding and when they were least active (to accomplish this they were given a "comfort" to suck). The infants were regarded as normal if the weight was not less than 20 per cent below the average for their age, and those weighing less than 20 per cent below the average were classified as hypothreptic. The total number of calories for twenty-four hours is plotted against the weight in kilograms for normal infants, and it is found that most of the results fall within 10 per cent above or below the average line; a somewhat greater variation, however, is present in the cases of some perfectly normal infants. During the first month of life the metabolism in calories per kilogram rises to the figure for about 6 kilograms. It remains fairly constant for that for from 6 to 10 kilograms and falls after the weight of the infant reaches 10 kilograms. The metabolism in calories per square unit of body surface rises in early infancy, remains fairly constant for several years and then gradually declines until adult life. Hypothreptic infants showed a higher caloric production per kilogram as well as per surface area than normal-sized infants. The low metabolism of new-born infants, which gradually rises in early life, is explained by the hypothesis that it takes the infant some time to adjust itself to the absence of the completely surrounding warm medium in utero in which the calories required are much less than in the environment after birth.

BENJAMIN, Montreal, Canada.

VARIATIONS OF BLOOD CHOLESTEROL IMMEDIATELY AFTER IRRADIATION WITH LIMITED RAYS. S. MALCZYNSKI, Compt. rend. Soc. de biol. **112**:925 (March 10) 1933.

Two series of dogs with shaved backs were exposed to the roentgen rays (with the Bucky diaphragm) at distances of 10 and 8 cm. for ten minutes. The average blood cholesterol of each group—172 and 158 mg.—was lowered to 160 and 152 mg., respectively. The reaction, therefore, is very feeble.

WAHL, Cleveland.

INFLUENCE OF ULTRAVIOLET IRRADIATION ON BLOOD SERUM CALCIUM AND POTASSIUM. C. ROSSO and A. CABITTO, Clin. pediat. **15**:835 (Nov.) 1933.

When normal dogs were given a single dose of irradiation with ultraviolet light the blood serum calcium increased, while the potassium decreased. After repeated exposures there was a decrease in both calcium and potassium.

DOOLEY, Kent, Conn.

THE PROGNOSIS OF ACETONEMIC VOMITING IN CHILDHOOD. R. TURQUETY, J. de méd. de Paris **54**:623 (July 19) 1934.

Turquety reports a case of cyclic vomiting with a fatal outcome in a girl, aged 7 years. She was in excellent health a few days before the onset and had had only four previous attacks. Findings which foreshadowed the fatal outcome were: the intensity of the vomiting, the early appearance of blood in the vomitus, marked albuminuria with cylindruria, dyspnea, hypothermia and cyanosis. These seem to be clinical manifestations of hepatonephritis, the infectious or toxic nature of which has not been determined.

LESLIE, Evanston, Ill.

CAUSES AND CLINICAL TYPES OF DYSTROPHIES IN HOSPITALIZED INFANTS. ANTONIO CARRAU, JULIO LORENZO Y DEAL and HECTOR MOURIGÁN, Arch. de pediat. d. Uruguay **4**:417 (Oct.) 1933.

More than 80 per cent of the infants admitted to the hospital are dystrophic. Breast fed infants rarely show the condition. Underfeeding and prematurity are the chief factors in producing the dystrophies. Infections are less frequently the cause. Otitis media is extraordinarily frequent in hospitalized patients with diarrhea. It often occurs within forty-eight hours after admission. It is very resistant to treatment.

Mastoiditis was not a common complication in the cases studied. Complications at birth and congenital syphilis ranked third in the list of causes. Constitutional factors played a minor rôle. Bad environment and poor housing conditions were common to nearly all the cases. Hospitalization per se was not a factor favoring the development of dystrophy. In the hospitalized infants both the acute and chronic disorders were generally relieved or permanently cured in the large majority of cases.

The authors consider dystrophy in infants one of their greatest problems. As prophylactic measures, they recommend: (1) breast feeding; (2) artificial feeding, with a diet adequate in both quantity and quality (excessive dilutions of the food must be avoided); (3) educational propaganda regarding the proper growth and development of the infant; (4) breast milk for the hospitalized infant and expert technical care, and (5) proper regard for meteorological factors during the hot seasons.

SCHLUTZ, Chicago.

CONTROL OF CONDENSED BREAST MILK: A p_H COLORIMETRIC METHOD FOR DETECTING ADULTERATION WITH COW'S MILK. JOSÉ OBES POLLERI and MARIANO C. SAIZAR, Arch. de pediat. d. Uruguay **4**:505 (Dec.) 1933.

As a new and accurate method of differentiating between human milk and cow's milk and as a test to detect adulteration of human milk with the latter, the authors suggest the use of bromthymol blue and phenol red.

A few drops of a 0.6 per cent solution of bromthymol blue added to human milk gives a greenish color, and in the presence of cow's milk a yellow color.

The phenol red reaction is as sensitive as the Moro reaction and makes it possible to detect adulteration of human milk with cow's milk in amounts as low as 10 per cent.

SCHLUTZ, Chicago.

RELATIONSHIP BETWEEN DIGESTIVE DISORDERS AND DISEASES OF THE THROAT. J. GUERRA ESTAPÉ, Pediatría españ. **21**:637 (Oct.) 1933.

The author points out the definite connection which exists between these two disorders. but believes that the relationship is characteristic for certain constitutional types. In advising tonsillectomy and adenoidectomy, he is influenced not so much by the hypertrophy of these structures as by the constitutional make-up of the child and certain disabilities which have developed, such as abnormalities of respiration and phonation and recurrent infections of the nose, ears and bronchial tract. He advises against indiscriminate operative procedure in the throat.

SCHLUTZ, Chicago.

TRANSFORMATION OF ERGOSTEROL TO VITAMIN D. O. F. F. NICOLA, Rev. de med., Buenos Aires **19**:479 (Feb.) 1934.

Nicola found that the principles of photochemistry, that is, the laws of distance from illumination, mass, intensity of luminosity and the like, apply to the transformation of ergosterol into vitamin D. He also agrees with the ideas of Bourdillon and Webster that the increase in optical density is particularly in the region of wavelengths of 295, 280, 270 and 245 millimicrons, and that irradiation with wavelengths of between 300 and 284 millimicrons gives a greater quantity of vitamin than that with wavelengths of between 280 and 254 millimicrons. This irradiation may give rise to other substances, but these do not appreciably affect the antirachitic effect of the vitamin. However, too long an irradiation of ergosterol destroys vitamin D.

SANFORD, Chicago.

THE APLONA (APPLE) DIET IN NUTRITIONAL DISTURBANCES IN INFANCY. H. A. SCHMIDT, Kinderärztl. Praxis **5**:17 (May) 1933.

Aplona is derived from fresh ripe apples which are dried and then reduced to powdered form. Heretofore the apple treatment has been employed only in children over 1 year of age, but the author tried aplona in sixty cases of nutritional disturbance in infancy, the ages of the patients ranging from 2 weeks to 9 months. The results were uniformly good.

HUENEKENS, Minneapolis.

ANTISCORBUTIC VALUE OF DOMESTIC SUMMER APPLES. H. PELC and M. PODZIMKOVA, Časop. lék. česk. **71**:1159, 1194 and 1223 (Sept. 9, 16, 23) 1932.

Pelc and Podzimkova compare the antiscorbutic value of summer, fall and winter apples, bananas and oranges. Five cubic centimeters of market orange juice in autumn and early winter was insufficient to protect experimental guinea-pigs when given as a daily supplement to a scurvy-producing diet. The daily addition of 20 Gm. of banana proved to be a good antiscorbutic, but does not assure full protection when the experiment is carried out over a long period. The domestic summer variety of apples did not appear to be a ready source of antiscorbutic vitamin. The antiscorbutic potency of autumn and early winter apples is much greater than that of early spring apples. Photographs and charts showing progress and weight are presented.

STULIK, Chicago.

STUDY OF THE CONTENTS OF CHOLESTEROL IN BLOOD SERUM IN HEALTHY AND SICK CHILDREN. JON ZIENKIEWICZ, Pedjatrja Polska **13**:175, 1933.

All together, 663 subjects were studied. Of these, 60 were pregnant women, 113 healthy children and 490 children with different diseases. There were 163 children with acute infectious diseases, 124 with chronic diseases, 29 with constitutional diseases, 11 with diseases of the blood and the blood-forming organs, 2 with metabolic diseases, 37 with gastro-intestinal diseases, 78 with diseases of the respiratory organs, 25 with genito-urinary diseases and 21 with nervous diseases.

The results were: In pregnancy there was hypercholesteremia up to three months; then the cholesterol rose up to nine months. In normal children the lowest amount of cholesterol was found in infants in the first month of life. This gradually rises to a normal level of about 1.5 per cent. In all the acute cases the cholesterol was diminished. In chronic diseases such as tuberculosis and congenital syphilis no definite changes were noted; however, in pulmonary tuberculosis with fever there was hypercholesteremia. In diabetes hypercholesteremia was found. In gastro-intestinal diseases there was a definite diminution of cholesterol, and in diseases of the respiratory organs also it was found that the cholesterol drops to a low level. In bronchial asthma, however, there was 3 per cent hypercholesteremia. In kidney disease the cholesterol was increased in mixed kidney infections. In nervous diseases the lowest amount of cholesterol was found in epilepsy.

KRUPINSKI, Chicago.

PROPHYLAXIS OF RICKETS. J. H. G. CARSTENS, Nederl. tijdschr. v. geneesk. **77**:4256 (Sept. 16) 1933.

With the modern methods of prophylactic treatment of rickets it is possible to prevent with certainty severe cases and the greater part of the mild cases. The factors which may increase the need of the organism of the child for vitamin D and which therefore may also indirectly promote the development of rickets are discussed. Recent experience has taught that the greater proportion of babies and young children may be protected against rickets by giving a small amount of vitamin D during the winter months. The great individual variation in the need for vitamin D, as well as individual variation regarding the dose and the time of application, makes necessary regular medical control of babies, in order to prevent part of the children from getting rickets notwithstanding the use of prophylactic measures.

VAN CREVELD, Amsterdam, The Netherlands.

Prenatal Conditions

CONGENITAL CLEFTS OF THE FACE AND JAWS: A SURVEY OF THREE HUNDRED AND FIFTY CASES IN WHICH OPERATION WAS PERFORMED. HARRY P. RITCHIE, Arch. Surg. **28**: 617 (April) 1934.

In this review of 350 cases especial attention was given to familial incidence and associated deformities. There were 34 cases with familial incidence and 26 cases with associated deformities. The combination and degree of the clefts were grouped. The first group contained 38 cases with a prealveolar process cleft. In this group the alveolar process and the hard and soft palates are normal. The defect is that of a cleft in front of a normal alveolar process. In this type of cleft the repair operation may be performed any time after feeding is established and the baby is gaining weight. The second group consists of cases of postalveolar process cleft. In this group the lip and the alveolar process are normally united. The hard and the soft palate are cleft in varying degrees. In this group there were 56 cases in which operation was performed. The average age at which operation was performed varied from 14 months to 2 years. The third group, consisting of cases of alveolar process cleft, shows many possible combinations. The combination determines the type of operation and the time of operation. In general, the repair of the alveolar process cleft should be done first as early as is compatible with the condition of the child. The repair of the lip is left to the judgment of the operator. Repair of the hard and the soft palate should be postponed to the second year or later, with particular attention to the season selected for operation. Only 5 infants died of the 350 operated on. The low mortality was attributed to the great care taken in selecting the proper time for operation. The results of operation on the various types of deformities are described.

KAISER, Rochester, N. Y.

SPINA BIFIDA AND CRANIUM BIFIDUM: A STUDY OF ONE HUNDRED AND THREE CASES. SIDNEY W. GROSS and ERNEST SACHS, Arch. Surg. **28**:874 (May) 1934.

A report is made of ninety-six cases of spina bifida in infants and young children and of five cases of cranium bifidum. Forty-six of the patients in this series were not subjected to operation. Of these, thirty-six died while in the hospital; the other ten had extensive defects associated with hydrocephalus and complete paralysis of the lower extremities. Fifty-seven patients were subjected to operation. Of this number, thirty-eight were discharged from the hospital, showing a high operative mortality. Follow-up examination revealed that patients with simple meningocele who did not have hydrocephalus or paralysis of the lower extremities prior to operation grew up normally and rarely had any permanent serious disability. In the total series operated on, almost 50 per cent developed normally.

KAISER, Rochester, N. Y.

CONGENITAL ANOMALIES OF METABOLISM WITH SPECIAL REFERENCE TO CYSTINURIA AND MYOPATHIES. ERWIN BRAND, Bull. New York Acad. Med. **10**: 289 (May) 1934.

Among the "inborn errors of metabolism" Garrod is quoted as including albinism, pentosuria, alkaptonuria, cystinuria, congenital porphyrinuria and congenital steatorrhea. Because of the familial character of muscular dystrophy and the striking disturbance in the creatine and creatinine metabolism observed in these patients and because of the possibility that it may be metabolic in nature, this disease is considered in the group of inborn errors of metabolism. In this paper cystinuria and the myopathies are discussed.

Cystine cannot be synthesized by the body. It is one of the essential amino-acids that must be supplied from without (in the food). Derivatives of cystine play an important rôle in the oxidation-reduction processes in metabolism, particularly in connection with the sulphur radical. While a loss of cystine in the urine may be considered a minor metabolic disease, the formation of cystine in the pelvis of the kidney predisposes to kidney block. Cystine stones have been reported in children even as young as 2 years.

In regard to the myopathies, it has been claimed that the excretion of creatinine bears some relationship to the muscular mass but not to the tone or acitivity of muscles. Also, patients with progressive muscular dystrophy showed a low output of creatinine and a high output of creatine (low creatine tolerance). The chemical principles involving the use of glycine to modify the creatine metabolism are discussed from the therapeutic standpoint of the myopathies.

JAHR, Omaha.

ATYPICAL CHONDRODYSTROPHY. JOSEPH WARKANY and A. GRAEME MITCHELL, J. Pediat. **4**:734 (June) 1934.

Warkany and Mitchell report the case of a 12 year old boy who presented features resembling both chondrodystrophy (Parrot) and osseous dystrophy (Morquio). The fact that the patient's condition seemed intermediate between chondrodystrophy and osseous dystrophy suggests that these two diseases may have a common basis.

LEMASTER, Evanston, Ill.

DIAPHRAGMATIC HERNIA. C. CONTAT, Ann. d'anat. path. **10**:1, 1933.

A case of congenital true diaphragmatic hernia in a boy 18 months old is presented. It was parasternal and bilateral. Only three similar cases have been reported. A discussion of diaphragmatic hernia follows. Congenital false hernia forms over 86 per cent of these cases, is five times more frequent on the left side, and affects boys more frequently than girls. It results from a failure of fusion of the diaphragm during the third month of fetal life. Congenital true hernia is characterized by a sac composed of thinned-out diaphragm. Several theories

regarding its formation indicate: diminished resistance of the diaphragm; asymmetrical development of the liver; anomalous and insufficient blood supply to the diaphragm with atrophy of the muscle fibers.

PERRY J. MELNICK. [ARCH. PATH.]

A PARTICULAR FORM OF CRANIOFACIAL MALFORMATION. A. KREINDLER and M. SCHACHTER, Paris méd. **2**:102 (Aug. 4) 1934.

In the case reported there was a new combination of malformations described in the syndromes of Crouzon, Apert and Vogt. A boy of 10 years had acrocephaly, facial asymmetry due to atresia of the left superior maxillary sinus, syndactalism and paralysis of the superior and external bulbar muscles of the left eye.

LESLIE, Evanston, Ill.

DEFORMITY OF THE CAUDAL VERTEBRAL COLUMN. KARL GOLDHAMER, Monatschr. f. Kinderh. **60**:269, 1934.

Photographs and roentgenograms of the skeleton and gastro-intestinal tract of a 7½ year old boy showed a marked defect in the development of the lower part of the spinal column, anomalies of the ribs and feet and the presence of megacolon.

GERSTLEY, Chicago.

EXPERIMENTAL FETAL INFLAMMATION. F. WOHLWILL and H. E. BOCK, Virchows Arch. f. path. Anat. **291**:864, 1933.

Previous study of human placentitis and fetal infection had established that the reaction of the fetal tissues is chiefly histiocytic. In this experimental study of fetal inflammation turpentine or suspensions of bacteria or of india ink were injected into the amniotic liquor of guinea-pigs or into the umbilical cord, skin, muscles or internal organs of the fetuses. The injections were made at various stages of pregnancy. Fetal sepsis was most often bronchiogenic, as had been previously observed in the human material, and resulted from the aspiration of infected amniotic fluid. A morphologic reaction to bacterial invasion was not observed in the fetuses until near the end of gestation and was macrophagocytic. A histiocytic reaction to turpentine and india ink was observed early in pregnancy and was similar to that which occurs in coelenterates. Even after development of the circulatory system the reaction was primarily histiocytic. Late in gestation a few cells of myeloid origin appeared, but this phenomenon was always preceded by a histiocytic reaction.

O. T. SCHULTZ, Evanston, Ill. [ARCH. PATH.]

Diseases of the New-Born

PATHOLOGY OF INTRACRANIAL HEMORRHAGE OF THE NEW-BORN. HARRY R. LITCHFIELD and THURMAN B. GIVAN, Arch. Pediat. **51**:186 (March) 1934.

On the basis of a review of the protocols of postmortem examination of infants over a period of one and a half years, Litchfield and Givan discuss the pathology of intracranial hemorrhage of the new-born. The general pathologic picture is that of hemorrhage, the striking characteristics being due to the fact that hemorrhage takes place where it affects a tissue which, when destroyed, does not recuperate. As a result, permanent injury is done, and permanent defects are left.

The article also contains reports of three cases.

WADDELL JR., University, Va.

PROPHYLAXIS OF IMPETIGO NEONATORUM. W. H. GUY and F. M. JACOB, J. A. M. A. **102**:840 (March 17) 1934.

The success of the method advocated by Guy and Jacob warrants its more widespread adoption. The method consists of a cleansing bath with sterile liquid petrolatum, following which the baby is thoroughly rubbed from the top of the

head to the soles with 2 per cent ammoniated mercury ointment before it is taken from the delivery room. In the nursery the baby is cleansed daily with sterile cotton seed oil, and the buttocks and anus are cleansed with cotton balls and cotton seed oil. Soap, water and powder are not used. Formerly, 5 per cent ammoniated mercury ointment was used. A few cases of chemical dermatitis occurred, but since the strength of the ointment was reduced to 2 per cent there have been no further cases.

BONAR, Salt Lake City.

THE SEDIMENTATION REACTION IN THE NEWBORN. SAMUEL L. ELLENBERG, J. Lab. & Clin. Med. **19**:944 (June) 1934.

In fourteen normal infants ranging in age from 2 to 10 days blood was obtained from the superior longitudinal sinus, and the speed of sedimentation of the erythrocytes was determined by the Linzenmeir method. It was found to range between seven and twenty-three hours, with an average of fifteen hours. There is a tendency for the sedimentation reaction to become less prolonged as the infant becomes older. This prolonged reaction is probably the result of the low fibrinogen content of the infant's blood.

MCMURRAY, Galveston, Texas.

RADIOGRAPHIC EVIDENCE OF LIVE BIRTH. MIRON HAJKIS, Lancet **2**:134 (July 21) 1934.

The author confirms the findings of Sydney Smith. Air is to be found in the stomach and intestines only if the child has breathed, and roentgenography of the lungs and intestinal tract provides the best proof of live birth.

LANGMANN, New York.

ASEPTIC FEVER IN THE NEW-BORN. R. SOTO IRIBARREN, Med. de los niños **35**:178 (June) 1934.

In the early days of life the temperature of the new-born is very unstable and may rise abruptly to 38.5 or 40 C. (101.3 or 104 F.) within one or two days. This elevation in temperature is called by the French aseptic fever and by the German school transitory fever of the new-born. The etiology of this condition has long been a matter of dispute, the German school contending that it is due to an absorption of toxins from the bowel produced by the change of the intestinal flora owing to the change from meconium to milk. French authorities, on the other hand, are inclined to believe that it is of traumatic origin. Recently, Waitz, in a study of thirty-eight cases, concluded from the history of difficult labor and the existence of nervous symptoms (such as tense fontanels and convulsive movements) and the results of spinal puncture that there exists an acute edema of the meninges followed by aseptic meningitis.

Other authorities attribute the condition to dehydration and have demonstrated the favorable effect of giving an abundance of water with sugar between nursings. Iribarren advances the theory that this unexplained fever that disappears within a few hours is of intestinal origin and cites the close relationship of disorders of the vegetative nervous system to the alimentary tract in infancy and childhood (reflex vomiting, reflex cough and reflex convulsions).

Fever in the new-born of longer duration and associated with cyanosis, muscular rigidity or nystagmus is more likely to be due to meningeal irritation. The probability that a temperature curve may be a sign of heredosyphilis was suggested in a former work.

DWYER, Kansas City, Mo.

NECROSIS ADIPOSA NEONATORUM. HARALD HARPØTH, Acta pædiat. **15**:259 (March 28) 1934.

A boy sickened on the third day of life with fever, rapid respiration and prostration. At the same time an extensive but sharply demarcated lesion appeared on both buttocks. The skin of this region became cyanotic, cold, dry, glistening and

rigid. There was no edema. Gradually the whole of both gluteal regions was involved. Diagnostic aspiration yielded neither fluid nor pus, but some yellowish débris exuded through the puncture wound. When an incision was made the base of the wound presented an appearance suggesting fat necrosis. Secondary infection followed. While extension of the original process ceased, the skin and subcutaneous tissue of the involved area underwent massive necrosis and separated, leaving a large, deep defect the base of which was dry, yellowish and avascular. The temperature remained subfebrile during the whole illness. Death occurred after seven weeks. A careful histologic examination was made post mortem. The anatomic diagnosis was "idiopathic fat-necrosis."

Since it seemed obvious to Harpøth that the common infections could be excluded, the differential diagnosis involved the three varieties of sclerema neonatorum, namely, sclerema adiposum, sclerema oedematosum and necrosis adiposa neonatorum. The last was selected, and the correctness of the choice was confirmed at autopsy.

Harpøth discusses briefly the confused problem presented by the phenomenon of hardening of the skin and subcutaneous tissues in the neonatal period. Unfortunately, he adds little to extend the etiologic knowledge of the subject. It does not appear that bacteriologic or chemical studies were carried out in the reported case.

McCune, New York.

Acute Infections

Outbreak of Erythema Infectiosum in Elmsford, N. Y. Phyllis S. Kerr and Edward H. Marsh, Am. J. Pub. Health **23**:1271 (Dec.) 1933.

In the spring of 1933 an outbreak of twenty-five cases of erythema infectiosum was observed in Elmsford, N. Y. All the patients were between the ages of 3 and 13 years. Fever was seldom present, though there was occasional redness of the throat. The eruption consisted of a reticulated erythema which was usually found on the arms and legs, but in a few instances on the upper trunk and neck. There was flushing of the cheeks in two cases, and one child had a distinct butterfly patch across the nose. There were four instances of multiple infection in one family. The incubation period varied from four to fourteen days. No mode of spread was determined.

McBryde, Durham, N. C.

Precipitated Toxoid as an Immunizing Agent Against Diphtheria. J. N. Baker and D. G. Gill, Am. J. Pub. Health **24**:22 (Jan.) 1934.

One hundred per cent of 197 children who gave positive Schick reactions showed negative reactions when tested from two to three months after a single injection of 1 cc. of alum-precipitated toxoid. Similarly, 99 per cent of 1,414 children on whom the Schick test had not previously been carried out gave negative reactions from two to three months following a single injection. In 16,289 injections it was believed that the reactions were no more severe than those following the injection of crude toxoid. Eight children showed abscess formation, while indurations lasting from one to three weeks were not uncommon.

McBryde, Durham, N. C.

Cutaneous Reactions in the Diagnosis of Undulant Fever. Jacob D. Goldstein, J. Clin. Investigation **13**:209 (March) 1934.

The endermic reactions of two hundred and fifty-three patients were tested by the intradermal injection of whole heat-killed organisms of Bacillus abortus. Of this group, 10.3 per cent reacted positively. The reactions of ninety-two patients were similarly tested with organisms of B. abortus which had been extracted with alcohol and ether; of this group 9.6 per cent reacted positively. The endermic reaction is recommended for use as a supplementary procedure for the diagnosis of undulant fever.

Guest, Cincinnati.

MALARIA IN THE NEWBORN. J. W. EPSTEIN, J. Pediat. **4**:251 (Feb.) 1934.

A 9 week old infant who was brought to the hospital in Cleveland because of chills and fever every third day was found to have malaria, as was shown by the finding of plasmodia in the blood. The mother, a native of Palestine, had emigrated to the United States eight years previously. She said that she had never had malaria. Examination of the mother revealed a palpable spleen but no organisms in the blood. According to the history, the infant had received mother's blood intramuscularly on the third day of life. Apparently malaria was transmitted to the infant by this procedure.

LEMASTER, Evanston, Ill.

RAT-BITE FEVER IN CHILDREN. FRANK VAN DER BOGERT, New York State J. Med. **33**:1379 (Dec. 1) 1933.

A case of rat-bite fever in a child 2½ years of age is reported. Three intramuscular injections of sulpharsphenamine were followed by recovery.

AIKMAN, Rochester, N. Y.

MEASLES IN FOUR CENTRAL NEW YORK COUNTIES FOR 1932. FREDERICK W. SEARS, New York State J. Med. **33**:1381 (Dec. 1) 1933.

Sears reports on the epidemic of 1932. Early publicity through newspapers, pamphlets and visits to the home are of great value. Immune serum and human parental blood were used to advantage.

AIKMAN, Rochester, N. Y.

THE BLOOD COUNT IN RUBELLA. JOHN VINCENT CARROLL, Lancet **1**:182 (Jan. 27) 1934.

Plasma cells, chiefly of the Marschalko type, were found in all of thirty patients with rubella. These cells appeared very early in the disease; the number increased generally up to the third day to about from 3 to 11 per cent and then gradually declined. Türk cells were often present, but were not so constant in appearance or so numerous as the plasma cells. Plasma and Türk cells were also found in measles, but not so constantly as in rubella.

LANGMANN, New York.

"WHOOPING-COUGH ECLAMPSIA." J. B. ELLISON, Lancet **1**:227 (Feb. 3) 1934.

The constant occurrence of severe and usually fatal convulsions in many epidemics of pertussis throughout the world has prompted most observers to regard them as an integral expression of the primary disease, whatever the primary pathologic basis may be.

At present there are five principal theories: the apoplectic, the spasmophilic, the meningo-encephalitic, the neurotoxic and the angiospastic. Of these the meningo-encephalitic and the angiospastic deserve most consideration.

Though the evidence cannot be stated here, there are strong epidemiological reasons for believing that many cases of eclampsia in pertussis occur through the combination of whooping cough and influenza. Even so, it is not necessary to assume the existence of definite encephalitis. Protracted nervous disturbances following convulsions are the exception rather than the rule. (In Ellison's series of seventy cases there were only two terminations: death, in 46, and complete and rapid recovery, in 24.)

LANGMANN, New York.

STUDIES ON THE NATURE OF ANTIDIPHTHERITIC IMMUNITY AMONG SOUTH AFRICAN BANTU BY MEANS OF THE SCHICK TEST AND ANTITOXIN TITRATIONS. E. GRASSET, South African M. J. **7**:779 (Dec. 9) 1933.

Because of the frequently expressed opinion that the black race enjoys a natural immunity against diphtheric infections, Grasset undertook the present investigation, and drew the following conclusions:

"(1) Antidiphtheritic immunity in Bantu, far from being an absolute racial immunity, is a specific acquired general and humoral immunity.

"(2) Although the non-susceptibility rate is consistently lower among Natives than among Europeans, curves show that the immunity in both races is governed by the same immunological laws.

"(3) After a temporarily high percentage of immune subjects among the newborn resulting from hereditary maternal immunity, the susceptibility rate rises rapidly to reach a maximum among infants of from 1 to 3 years, followed by a progressive decline to reach a minimum among adults, this being governed by the daily immunity contact rate.

"(4) Without excluding the possible influence of a racial factor, we consider that to a great extent the high rate of immunity among Natives is due to their social conditions of life, leading to an early contact with the diphtheria bacillus, and consequently the production of an early specific immunity."

GONCE, Madison, Wis.

PROPHYLAXIS OF DIPHTHERIA AMONG INFANTS IN INSTITUTIONS. P. LEREBOULLET, Rev. franç. de puéricult. **2**:1 (Feb.) 1934.

In the infant under 1 year of age diphtheria is seen less often in its classic form than as diphtheritic coryza, catarrhal or membranous conjunctivitis, athrepsia or cholera-like diarrhea. Nasal cultures of infants admitted to the Hospice des Enfants-Assistés in Paris taken as a routine showed approximately 10 per cent to be diphtheria carriers. In 1927 the mortality among these carriers was 56 per cent. In 1928 a system of nasal culture for all the infants admitted and of isolation and disinfection of the carriers was inaugurated. In 1929 the mortality among the one hundred and one carriers was only 7 per cent, although the general mortality for infants in the hospital was 11 per cent.

CRANE, Chicago.

MENINGOMYELITIS CAUSED BY THE ORGANISM OF UNDULANT FEVER (BACILLUS ABORTUS). KNUD H. KRABLE, Rev. neurol. **1**:34 (Jan.) 1934.

Krabbe points out that it has been long known that the toxins of Malta fever have a particular affinity for the nervous system. The bovine strains do not, however, have this affinity. He summarizes two cases of meningomyelitis caused by Bang's bacillus, which have been reported in the Scandinavian literature, and adds a case of his own.

DAFFINEE, Boston.

COMPLICATIONS AFFECTING THE NERVOUS SYSTEM IN VARICELLA. D. CORDA, Arch. ital. di pediat. **2**:286 (Jan.) 1934.

Corda reports three cases of nervous manifestations complicating varicella. The first is that of a 21 month old baby who had paralysis of the right leg on the eighteenth day of the disease and recovered; the second, that of a 3 year old child who presented signs of cerebellar ataxia beginning on the sixth day and recovered, and the third, that of a 4 year old child who showed encephalitis on the sixth day and died. This article includes an exhaustive review of the subject.

DOOLEY, New York.

CONTRIBUTION TO THE STUDY OF CARDIAC INVOLVEMENT IN SCARLATINA WITH PARTICULAR REFERENCE TO THE MYOCARDIUM. WILLY SCHWARTZ, Pediatria **42**:267 (March 1) 1934.

Sixty-five patients with scarlet fever were observed clinically and electrocardiographically. These observations extended during the illness and a few weeks after the disease. The clinical findings of inorganic nature in these subjects were confirmed, but electrocardiograms revealed no myocardial changes in any case. Chronic valvular cardiac disease may be the consequence of scarlatinous endocarditis, according to the conclusions of Schwartz. He points out that the severity of the epidemic remains an important factor in relation to the frequency, severity and effect of cardiac complications.

SIGNORELLI, New Orleans.

PROPHYLACTIC ANTIDIPHTHERITIC MEASURES: CLINICAL AND EXPERIMENTAL RESULTS OF VACCINATION WITH ANATOXIN. E. MERLINI, Riv. di clin. pediat. **32**:163 (Feb.) 1934.

Merlini gives a résumé of the experience at the Provincial Orphanage at Genoa over a period of five years with diphtheria, diphtheria carriers and immunization against diphtheria.

The nasal route was first used in immunizing with anatoxin; later, hypodermic injections were substituted. Tests made during the first year after immunization showed that 2 per cent of the children had a positive Schick reaction; during the second year 11 per cent had a positive reaction; during the third year, 19 per cent, and during the fourth year, 17 per cent. Merlini believes that immunization against diphtheria should be compulsory for children of preschool age in institutions.

HIGGINS, Boston.

ETIOLOGY OF PUSTULOSIS VACCINIFORMIS ACUTA (KAPOSI-JULIUSBERG). HELMUTH FREUND, Dermat. Wchnschr. **98**:52 (Jan. 13) 1934.

A 2¼ year old child had had a dry, scaly skin since birth and eczema for one year. A sudden rise of temperature (to 41 C., 105.8 F.) occurred, as well as general adenopathy and an acute eruption of vacciniform lesions chiefly on the hands and face. New crops of cutaneous lesions appeared on the fourth and eighth days, with a moderate increase in temperature each time. The lesions cleared under applications of soothing ointments in less than three weeks. There was no history of exposure to vaccinia. Material from a fresh lesion was inoculated into the scarified surface of a rabbit's cornea, causing keratoconjunctivitis. Material from this rabbit was similarly inoculated into a second animal, and the eye was removed and sectioned two days later. Many Guarnieri bodies were demonstrated. After the complete recovery of the baby, vaccination was readily accomplished. The presence of the Guarnieri bodies indicates vaccinia, but the lack of resistance to vaccine contradicts this. The possible explanations for the contradictory facts are discussed.

TAUSSIG, San Francisco. [ARCH. DERMAT. & SYPH.]

INFLUENCE OF SPEED OF NEUTRALIZATION AND FLOCCULATION ON THE THERAPEUTIC ACTION OF DIPHTHERIA SERUMS. W. KOLLE and R. PRIGGE, Med. Klin. **30**:258 (Feb. 23) 1934.

It has been suggested that diphtheria serums which rapidly flocculate and readily neutralize toxins in vitro may be most effectual in treating the disease. Kolle and Prigge sought to test this suggestion by comparing the therapeutic effect of numerous serums on rabbits which had been inoculated with toxin either subcutaneously or intravenously. They conclude that the therapeutic effect of diphtheria serum depends on the time at which the serum is injected in relation to the onset, and not on the rate of flocculation or neutralization.

DOOLEY, New York.

ACUTE PURULENT OTITIS MEDIA WITH DIPHTHERIA. E. BERGH, Monatschr. f. Ohrenh. **68**:1 (Jan.) 1934.

In this report Bergh reviews the cases of otitis media occurring in 2,425 patients suffering from diphtheria observed from 1921 to 1930. Acute disease of the middle ear occurred in 121. It was one-sided in 61.2 per cent. There was considerable variation in the frequency of otitis as a complication of diphtheria both from year to year and in different seasons. The third quarter of the year showed the lowest incidence of otitis. The largest number of cases of diphtheritic otitis occurred between the first and sixth years of life, although the largest number of patients having diphtheria were aged from 6 to 8. The frequent occurrence of otitis in diphtheria falls from the first to the ninth year (with the exception of the eighth), and after this year the incidence is slight. Without doubt nasal diphtheria is more dangerous from the standpoint of complication with otitis

than diphtheria of the throat. About half the cases of otitis occurred after the twenty-first day of the diphtheria. The appearance of otitis has no influence on the mortality from diphtheria, but there was a parallelism between the mortality rate and the frequency of complications in the middle ear. In about two fifths of the patients with diphtheritic otitis the course is afebrile. The prognosis in this type of otitis is good in regard to life and to mastoid complications. Attempts to prevent complications in the middle ear as a result of diphtheria should be based on careful hygiene of the upper respiratory tract and especially of the nose.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

TREATMENT WITH DIPHTHERIA ANTITOXIN IN PRACTICE. RIETSCHEL, München. med. Wchnschr. **80**:1927 (Dec. 8) 1933.

Rietschel does not agree with the recently revived idea of Bingel that normal horse serum is as effective as antitoxin in the treatment of diphtheria. The value of diphtheria antitoxin has been demonstrated clinically and experimentally. Death in most cases is due primarily to vascular disturbance and secondarily to cardiac injury. The former may be the result of toxic action on the blood vessels, vasomotor center or endocrine glands (the suprarenals or hypophysis). Treatment is of little value, although camphor may be helpful. Digitalis is contraindicated in the acute stage.

Whether the severe form of diphtheria is due only to the toxemia or to the effect of a mixed infection with streptococci is still not settled. Cases in which no mixed infection can be demonstrated bacteriologically show the same clinical features as those in which streptococci are cultured. The presence of streptococci may enhance the production of toxin, increase the degree of absorption or increase the avidity of tissues for the toxin.

Early clinical diagnosis and early administration of serum are essential to reduce the mortality. Rietschel advises giving from 4,000 to 20,000 units of antitoxin, depending on the severity of the case. If serum is given after the third day, 10,000 units should be the minimum. Combining streptococcic serum with the diphtheria serum is worthless. Antitoxin acts most rapidly when given intravenously. However, any excess of antitoxin is quickly excreted, and for this reason Rietschel either combines the intravenous injection with an intramuscular injection or gives all the serum intramuscularly.

In the treatment of diphtheritic croup the general practitioner should not attempt intubation or tracheotomy. The fresh air treatment, with large doses of sedatives, is advised. Inhalations of steam may be given for short intervals. If the patient does not improve, suction of the membrane from the larynx is advised, a procedure which the author apparently considers simpler than intubation.

The possibility of anaphylactic shock from injection of serum in patients who have previously had serotherapy is considered. Rietschel suggests injecting 0.5 cc. of serum; if no reaction occurs within an hour, the rest of the serum may be given. Serious reactions are rare and have been overemphasized in textbooks. The antitoxin titer of serum from cows and sheep is low, and large quantities must be administered. There is greater danger of severe reaction from such serum than from horse serum.

BRAHDY, Mount Vernon, N. Y.

BLANCHING PHENOMENON IN SCARLET FEVER. W. WIECK, München. med. Wchnschr. **81**:94 (Jan. 19) 1934.

Wieck obtained serum from patients between 40 and 90 years of age who, according to their history, had not had scarlet fever. He also obtained serum from patients convalescing from scarlet fever. The two kinds of serum were used in carrying out the Schultz-Charlton test. A higher percentage of positive reactions were obtained with the normal serum than with the convalescent serum.

BRAHDY, Mount Vernon, N. Y.

AUTO-INFECTION OF DIPHTHERIA CARRIERS. H. LAUSECKER, München. med. Wchnschr. **81**:213 (Feb. 9) 1934.

Two children, aged 8 and 9 years, with scarlet fever, were admitted to the hospital. Both had positive Schick reactions, and diphtheria bacilli were found in the nasal cultures. In one child a diphtheritic infection (confirmed by cultures) was superimposed on a reaction vaccination against smallpox which had been performed a week before. The condition improved following local application of 16,000 units of antitoxin. A month later there was an infiltration at the site of the lesion, and the Schick reaction was still positive. An injection of 6,000 units of antitoxin was given and the indurated area disappeared within three days.

At the time of admission the second child had excoriated lesions at the side of the mouth. Five days after admission small vesicles developed at the corners of the mouth; these were soon covered by a membrane. The lesion spread to the lips and tongue. Diphtheria bacilli were found on culture. After the injection of 16,000 units of diphtheria antitoxin there was rapid healing.

BRAHDY, Mount Vernon, N. Y.

RESTRICTING THE SPREAD OF TYPHOID AND PARATYPHOID BY CARRIERS OF THE BACILLI. VICTOR GEGENBAUER, Wien. klin. Wchnschr. **47**:163 (Feb. 9) 1934.

Gegenbauer states that there are three chief methods for restricting the spread of typhoid fever and paratyphoid fever by carriers of the bacilli: (1) legal measures, (2) therapeutic treatment of the carriers and (3) hygienic care of water, sewage and milk and a hygienic mode of living. He considers the third method the most important.

In Vienna known carriers of typhoid fever and paratyphoid fever must register their name, address and place of work; they must have their clothes and bed linen disinfected, and they must not handle food, especially milk. Supervision of the carriers is discontinued only after monthly tests of the stools and urine have given negative results for an entire year.

The therapeutic treatment of carriers may be either internal or operative. Operative measures can hardly be considered as a means of restriction. One can hardly expect a single carrier to submit to operation when the majority of carriers are not subjected to any therapeutic or legal measures.

ARTHUR F. ABT, Chicago.

A CASE OF SEROUS MENINGITIS FOLLOWING VARICELLA. Y. KIMURA, J. Orient. Med. **21**:7 (July) 1934.

Five days after the onset of varicella, a girl, 4 years old, had somnolence, repeated vomiting, headache and paralysis of both legs, with, however, no increase in temperature. The pulse was slow and the breathing irregular. The knee jerks were absent, and some ataxia was present. The neck was not stiff, and Kernig's sign was negative. The spinal fluid showed increased pressure, fine granules, a slight increase in lymphocytes (24 per cubic centimeter) and no increase in protein. The Nonne-Apelt reaction was negative in phase I; Pandy's reaction was positive; the sugar was slightly increased, and there were no bacteria. The symptoms gradually disappeared, and within twenty days the child was normal.

EDITOR'S SUMMARY.

PROPHYLAXIS AGAINST SCARLET FEVER BY INHALATION. G. ISHIYAMA, J. Orient. Med. **21**:24 (Aug.) 1934.

Ishiyama, in investigating an inhalation method of prophylaxis against scarlet fever, compared the agglutination titer of lung extract and blood serum obtained from puppies following the intratracheal, the intravenous and the subcutaneous injection of hemolytic streptococci. The building of agglutinins in the lung extract was much greater following the intratracheal injection; the building of agglutinins

in the blood was slightly less following this method than when the intravenous route was used, but greater than that following the use of the subcutaneous route.

EDITOR'S SUMMARY.

CLINICAL OBSERVATIONS OF TYPHOID AND PARATYPHOID FEVER IN CHILDREN WITH SPECIAL REFERENCE TO THE DISTRIBUTION OF THE BACILLI. G. SANO, J. Pediat. (Tokyo), Jan. 20, 1934, no. 404, p. 9.

Sano made observations on seventy-one children with typhoid fever and twenty-seven with paratyphoid fever. He found that the Widal reaction was positive in 85 per cent of those with typhoid fever and 90 per cent of those with paratyphoid fever at the end of the first week after the onset. A blood culture was positive in 83 per cent of those with typhoid fever and 100 per cent of those with paratyphoid fever at the same period. Positive cultures of the urine were obtained in 18 per cent of those with typhoid fever and 19 per cent of those with paratyphoid fever, while cultures of stools were positive in 57 per cent of those with typhoid fever and 39 per cent of those with paratyphoid fever. Bacteremia, as tested by positive cultures, was present in 100 per cent of those with paratyphoid fever during the first eight days of illness and in from 60 to 90 per cent of those with typhoid fever. The positive cultures in cases of typhoid fever from the ninth to the fourteenth day of illness were only one third as many as were obtained during the first eight days, while in the cases of paratyphoid fever all the cultures were negative during this period. The bacilli were excreted in the urine in the greatest number of cases (40 per cent) during the period from the twenty-second to the twenty-fourth day of illness, and no positive cultures were obtained during the first two weeks. The excretion of bacilli in the stools seemed to occur during the second and third weeks.

KATO, Chicago.

PSEUDO-REINFECTION WITH PERTUSSIS. I. INABA, J. Pediat. (Tokyo), Feb. 20, 1934, no. 405, p. 143.

Inaba made extensive clinical and hematologic observations in four cases of so-called recurrent attacks of whooping cough and concludes that in all the patients the whooping type of cough recurred whenever there was infection of the upper respiratory tract, but there was no characteristic lymphocytosis.

KATO, Chicago.

DIPHTHERIA OF THE SKIN. AAGE KRISTJANSEN, Hospitalstid. (supp.) **76**:17 (Dec. 21) 1933.

A 5 year old boy had a severe form of prurigo of the Besnier type, with pronounced eczema of the face and scalp, which had proved resistant to all ordinary treatment. He had spent his third and fourth years in frequent transfers between the hospital for diseases of the skin and the hospital for contagious diseases. Invariably examination at the former revealed the presence of diphtheria bacilli in the discharge from the nose and throat and at the roots of the hairs, and he was transferred to the latter. When examination at the hospital for contagious diseases no longer showed diphtheria bacilli he was sent back to the hospital for diseases of the skin, whence after a few weeks or months he was returned to the hospital for contagious diseases. When he was seen by Kristjansen diphtheria bacilli were found at the roots of the hair. Here could be seen and felt numerous nodular infiltrations, groups of follicular pustules and tiny abscesses; on puncture the abscesses proved to be filled with pus containing diphtheria bacilli. The bacillary infection was refractory to treatment with poultices, salves, ichthyol, serum and other remedies. An epilation dose of the roentgen rays was applied, and afterward the scalp was painted with a 1 per cent solution of acriflavine hydrochloride, which caused the pustules to dry up completely. At the Municipal Serum Institute three months later the skin yielded rolls of diphtheria bacilli, cultivation of which produced a very toxic virus.

VINTON, Brooklyn.

IMMUNIZATION AGAINST DIPHTHERIA AND SCARLATINA IN THE TOWN OF HAARLEM DURING 1929 TO 1933. W. J. H. MASCHHAUPT, Nederl. tijdschr. v. geneesk. **78**:1123 (March 10) 1934.

In Haarlem in 1929 to 1932 satisfactory results were obtained in immunization against diphtheria by means of toxin-antitoxin. No difficulties were reported.

The results of the immunization in 1933 with mixed antidiphtheria and antiscarlatina vaccine were satisfactory. The vaccination gave rise to a variety of symptoms, such as fever, vomiting and a strong local reaction, and fifteen cases were not distinguishable from true scarlet fever. After a new injection of this vaccine the symptoms suddenly stopped. No contagion was reported. On the basis of this, the condition was assumed to be due to the toxin, and not to be of bacterial origin. Because of the many difficulties, it was decided to return to the toxin-antitoxin preparation.

VAN CREVELD, Amsterdam, The Netherlands.

Chronic Infections

A TUBERCULOSIS SURVEY IN MENTAL HOSPITALS. B. T. MCGHIE and G. C. BRINK, Am. J. Psychiat. **13**:925 (March) 1934.

Patients in hospitals for persons with mental disorders show a higher incidence of tuberculosis than the general hospital population or the population in general. Mentally defective children show a special susceptibility to tuberculosis, as revealed by physical and roentgen examinations and tuberculin tests.

Eight hundred and eighty-six patients selected from a population of 10,500 patients were studied. The study covered a period of five years.

JAHR, Omaha.

TUBERCULOSIS OF THE THYROID GLAND WITH REPORT OF A CASE IN A CHILD AGED THREE. L. M. LINDSAY and C. I. MEAD, Canad. M. A. J. **30**:373 (April) 1934.

A review of the literature is given. Most patients with tuberculosis of the thyroid gland who came to autopsy showed tuberculous lesions in other organs, chiefly in the lungs and cervical lymph glands.

In the case reported the patient showed three of the more unusual manifestations of tuberculosis in children: a caseous type of tuberculosis of the thyroid, a tuberculoma of the epicardium and a solitary tuberculoma of the brain.

The patient was a colored boy of 3 years, with frequent familial contact with tuberculosis. He had intermittent convulsions beginning at the end of the first year. He was admitted to the hospital with symptoms of nasal discharge, fever, cough, anorexia and loss of weight. Physical examination showed evidence of bronchopneumonia of the lower lobe of the left lung and, in addition, a firm mass located in the region of the left lobe of the thyroid gland. The course was rapidly progressive, and the child died one month after admission. Complete details of the autopsy are given.

MOORE, Omaha.

AN EXPERIMENTAL STUDY OF META-AMINO PARA-HYDROXY PHENYL ARSINE OXIDE AS AN ANTISYPHILITIC AGENT. A. L. TATUM and G. A. COOPER, J. Pharmacol. & Exper. Therap. **50**:198 (Feb.) 1934.

Tatum and Cooper compare this arsenical with the arsphenamines, discussing the chemical, toxicological and therapeutic properties. It is a pure compound; it becomes less toxic on oxidation and is much simpler to prepare for clinical use.

PILCHER, Cleveland.

PHYSICAL SIGNS AS A MEASURE OF ACTIVITY IN PULMONARY TUBERCULOSIS. FRANK H. HUNT, New England J. Med. **211**:239 (Aug. 9) 1934.

Hunt believes that physical signs alone are at all times inadequate and are often absolutely misleading. Unfortunately, too many cases are seen in which are found clearing up of the original process and corresponding improvement in the patient, but in which a roentgenogram, while confirming these physical findings, reveals a new infiltrative lesion in another part of the lung. The reverse of this picture may be seen, though not so frequently. GENGENBACH, Denver.

THE X-RAY IN THE MEASUREMENT OF ACTIVITY IN PULMONARY TUBERCULOSIS. OLIN S. PETTINGILL, New England J. Med. **211**:240 (Aug. 9) 1934.

The information conveyed by one flat film or by well taken stereoscopic films is of far less value than serial films, in the same proportion as a complete physical examination of a patient is to the observation of that patient in a known environment. The value placed on the roentgenogram in the study of activity in resident patients at Essex Sanatorium is shown by the increase in the number of serial roentgenograms taken each year. Ten years ago the average was one film per patient every ten months; last year the average was one film per patient every four months. Correlation of the shadows on the x-ray films with the physical signs, laboratory findings, complications, age, sex and constitutional disturbance is necessary to complete the interpretation.

The roentgenogram usually reveals the presence of pulmonary tuberculosis and the progress of the disease earlier than physical signs or symptoms. The lesion that appears on the film as a dense shadow with a clearcut, abrupt margin, sometimes isolated and showing no change over a period of years, may be considered arrested. GENGENBACH, Denver.

THE LEUCOCYTIC PICTURE AS AN AID IN THE MEASUREMENT OF ACTIVITY IN PULMONARY TUBERCULOSIS. JACOB KAMINSKY, New England J. Med. **211**:245 (Aug. 9) 1934.

Kaminsky studied a group of tuberculous patients by taking frequent total and differential blood counts during the past two years. More than 1,200 total and differential counts were done. It was found that the leukocytic pictures may be in close agreement with the clinical and roentgen findings throughout the course of observation in a given case. Since experience has shown that patients who show exacerbations of their lesions have had septic blood pictures all along or that their pictures have reverted to the septic type, it would seem justifiable to regard a septic blood picture as a sign of activity, even though the clinical and roentgen findings point in the other direction. GENGENBACH, Denver.

A NOTE ON THE STUDY OF PULMONARY TUBERCULOSIS IN INFANTS AND CHILDREN. G. GREGORY KAYNE, Brit. M. J. **1**:370 (March 3) 1934.

This article describes the technic of diagnosing tuberculosis in infants and young children both during life and at autopsy. Certain difficulties representing various opinions are outlined. The importance of the social history, with the possibility of contact in view, is stressed. Clinical examination includes (*a*) physical examination; (*b*) taking roentgenograms of the chest, both in the anteroposterior and in the lateral or oblique position, and (*c*) doing a tuberculin test. It is noteworthy that the Pirquet test was used exclusively by Kayne. Finally, search for tubercle bacilli is made by washing out the stomach. The necropsy material is studied along the well known lines of Armand-Delille, with whom Kayne has studied. ROYSTER, University, Va.

ON THE LACK OF EVIDENCE OF TRANSMISSION BY HUMAN BEINGS OF TUBERCULOSIS DUE TO THE BOVINE TYPE OF BACILLUS. GILBERT WALKER, Brit. M. J. **1**:371 (March 3) 1934.

A study was made to determine any possible evidence of transmission by man of tuberculosis caused by the bovine type of bacillus. Walker's conclusions are as follows:

"There is no proof that spread of bovine type tuberculosis by humans occurs.

"There are opportunities for contact infection under conditions similar to those which cause spread of tuberculosis due to human type bacilli.

"It is suggested that the bovine bacillus has a lower invasive capacity than the human, and produces progressive disease less readily."

ROYSTER, University, Va.

RAYNAUD'S DISEASE AND HEREDITARY SYPHILIS. N. J. SPYROPOULOS and G. GEORGARAS, Arch. de méd. d. enf. **37**:77 (Feb.) 1934.

The syndrome of Raynaud has usually been considered from a pathogenic rather than from an etiologic point of view. In recent years, however, numerous authors have included congenital syphilis as a factor in the production of arterial spasm complicating endarteritis. Giroux, for example, found fourteen instances of inherited syphilis among forty-two cases of Raynaud's disease, and asserted that this infection must be classed with the primary etiologic agents in the genesis of symmetrical gangrene of the extremities.

The authors report a case of this condition in a girl, 2½ years of age. The child lived in an insanitary environment on the outskirts of Athens and was brought to the hospital suffering from the syndrome of Raynaud; the toes of both feet were affected. The Wassermann reaction was strongly positive, and the condition yielded promptly to antisyphilitic treatment.

AMESSE, Denver.

PREVENTION OF TUBERCULOSIS IN CHILDHOOD. WALTER PEIRIS, Bull. Assoc. internat. de pediat. prevent. **1**:21 (Sept.) 1934.

Writing from Ceylon, Peiris states that 40,000 American children die annually of tuberculosis; that 80 per cent of the children of Paris are infected, and that 92 per cent of all cases of tuberculosis in Ceylon are of the pulmonary type. He urges the necessity of employing to the utmost all official and unofficial agencies in a campaign of prevention. The special features to be emphasized in this vital movement are: the pasteurization of milk, with repeated testing of dairy herds; preventoriums for contacts; oral hygiene; respiratory exercises and postural corrections, better after care in measles and whooping cough, and control of the patent medicine industry.

AMESSE, Denver.

TUBERCULOUS ETIOLOGY OF ERYTHEMA NODOSUM. RAÚL CIBILS AGUIRRE, Arch. argent. de pediat. **4**:617 (Sept.) 1933.

The author discusses at some length the various opinions held regarding the etiology of this disorder and reports twelve cases in patients ranging in age from 2 to 14 years. Very young children are infrequently affected. The author is convinced from his own personal experience that almost without exception the etiologic factor in every case can be proved to be tuberculous.

SCHLUTZ, Chicago.

GENITAL TUBERCULOSIS IN EARLY INFANCY. MARTINEZ VARGUS, Med. de los niños **35**:129 (May) 1934.

A case of tuberculosis of the epididymis with incipient orchitis is reported in a boy, aged 28 months. The tumefaction of the testis appeared at the age of

7 months. The Pirquet and Mantoux reactions were positive, and there was roentgenographic evidence of tuberculosis in the peribronchial glands.

The treatment consisted of surgical extirpation followed by galvanocautery.

A colored drawing and two colored photomicrographs illustrate the lesion. The literature is reviewed, and the rarity of genital tuberculosis in infancy is emphasized.

DWYER, Kansas City, Mo.

Internal Diseases

TREATMENT OF AMEBIC DYSENTERY. HORACE W. SOPER, Am. J. Digest. Dis. **1**: 58 (March) 1934.

Soper reports that emetine used in conjunction with acetarsone seemed a specific in the treatment of seventy-five patients with early amebic dysentery. One grain (0.06 Gm.) of emetine was given intravenously daily for seven days. Then one tablet of acetarsone was given three times daily before meals, which was followed by the intravenous injection of emetine once a week for three weeks. A proctoscopic examination was made at each visit. No severe reactions were noted during the administration of emetine. Some patients experienced a feeling of giddiness and fulness in the head immediately after the injection of the drug.

Soper also calls attention to the fact that all patients do not show Endamoeba histolytica in the stools and believes that proctoscopic examination should be included in the routine. One practically always finds the ulcers, even in early cases, and Endamoeba histolytica is recovered from the scrapings of the ulcers.

MORRISON, Savannah, Ga.

PRIMARY CARCINOMA OF THE LIVER IN INFANCY—REPORT OF AN INSTANCE. RALPH A. KORDENAT, Am. J. Digest. Dis. **1**:60 (March) 1934.

A case of primary solitary carcinoma of the liver in a boy, 11 months of age, is reported. The complete observations at autopsy are recorded. A review of the literature concerned with primary malignant process of the liver is given.

MORRISON, Savannah, Ga.

REPORT OF A CASE OF NON-LIPOID HISTIOCYTOSIS (RETICULOENDOTHELIOSIS) WITH AUTOPSY. NATHAN CHANDLER FOOT and CHARLES T. OLCOTT, Am. J. Path. **10**:81 (Jan.) 1934.

A case of non-neoplastic proliferation of the retothelium without the lipoid changes of lipoid histiocytosis in a 3 year old girl is reported. The term non-lipoid histiocytosis or reticulo-endothelosis is proposed for this rather rare disease, which was first described by Borissowa in 1903. The two theories of the nature of the disease, inflammatory and leukemic, are discussed.

MOORE, New York.

THE VISCOSITY OF LIPIODOL IN BRONCHOGRAPHY. ROBERT G. BLOCH, Am. J. Roentgenol. **27**:847 (June) 1932.

The distribution of oil in the undiseased lung carries the possibility of infection and of diagnostic errors. Two cases in which the instillation of iodized poppy-seed oil 40 per cent and bronchography revealed lesions which subsequently were not verified are reported; one was a case of bronchiectasis and the other a case of tuberculosis. Several experiments showing the viscosity of iodized poppy-seed oil at various temperatures are cited. When too cold, iodized poppy-seed oil, in addition, produces a cough reflex which prevents proper filling. Bloch thinks that the oil should be injected at a temperature between 20 and 25 C. (68 and 77 F.). Down to 20 degrees the oil is warm enough not to irritate the upper airways, and the flow occurs with sufficient slowness. Alveolar filling and roentgenographic after-effects in the pulmonary field will thereby be largely avoided. A water-bath apparatus is shown, with details for its use. In this, the oil is kept at the proper temperature until the operator is ready to make the injection.

STULIK, Chicago.

SPLANCHNIC NERVE SECTION IN JUVENILE DIABETES: I. SELECTION OF CASES FOR OPERATION. G. DE TAKÁTS, G. K. FENN and RUTH A. TRUMP, Ann. Int. Med. **7**:1201 (April) 1934.

The authors discuss the various factors that influence sensitivity to insulin in animals and tabulate these with regard to their ability to increase or decrease sensitivity to insulin. A test is described for determining this sensitivity as well as the effect of ergotamine on galactose hyperglycemia, and the value of these tests in relation to operability are discussed. The immediate aim of operative procedures on diabetic patients, if the condition is resistant to insulin, is to increase the sensitiveness to insulin. It is pointed out that resistance to insulin occurs, but is rare, in children, and it is this group which is resistant to insulin and sensitive to ergot that obtains great benefit from section of the splanchnic nerve.

READING, Galveston, Texas.

"ALLERGIC" SHOCK: III. FROM SUBSTANCES OTHER THAN POLLEN AND SERUM. GEORGE L. WALDBOTT, Ann. Int. Med. **7**:1308 (April) 1934.

In this article reference is made to previous contributions expressing the author's belief that so-called "thymic" death is in reality due to "allergic" shock. In support of this assumption the work of Landsteiner and that of Avery are cited to substantiate his belief that antigenic qualities do not depend on whether or not a substance contains protein. It is stated that local and general anesthetics may give rise to atopic symptoms and that sudden death following anesthesia may well be explained on this basis. The author reports seven cases of allergic shock caused by substances other than pollen and serum.

READING, Galveston, Texas.

HYPERPARATHYROIDISM (RECKLINGHAUSEN'S DISEASE OF BONE). HENRY L. JAFFE, Arch. Path. **16**:236 (Aug.) 1933.

This article is a continuation of a general review of hyperparathyroidism begun in the *Archives of Pathology* (**16**:1 [July] 1933). The discussion includes the symptoms, serum calcium, serum phosphorus, mineral metabolism, serum phosphatase, roentgenographic changes in the bones, differentiation from other malacic diseases and surgical and medical treatment of this condition.

LEMASTER, Evanston, Ill.

THE INFLUENCE OF ADRENAL CORTEX EXTRACT ON THE RESISTANCE TO CERTAIN INFECTIONS AND INTOXICATIONS. W. S. M. SCOTT, W. L. BRADFORD, F. A. HARTMAN and O. R. MCCOY, Endocrinology **17**:529 (Sept.-Oct.) 1933.

Because it has been shown that the administration of extract of the suprarenal cortex benefits the diminished resistance to certain bacterial intoxications of animals the suprarenal glands of which had been removed; the effect of such an extract in animals with intact suprarenal glands was tried. The effect of diphtheria toxin on the guinea-pig, Trypanosoma equiperdum on the rat and Pneumococcus on the mouse was noted in animals treated with extract and in controls. No benefit was demonstrated from the doses of cortical extract used.

JACOBSEN, Buffalo.

DETERMINATION OF THE SPECIFIC DYNAMIC ACTION OF PROTEIN AND ITS VALUE IN THE DIAGNOSIS OF PITUITARY DISEASE. M. A. GOLDZIEHER and M. B. GORDON, Endocrinology **17**:569 (Sept.-Oct.) 1933.

It has been known for a number of years that the specific dynamic action of proteins is reduced in obesity, and it has been suggested that this may be due to an underlying deficiency of the anterior lobe of the pituitary gland. Some have noted an increase in specific dynamic action following the administration of extract of the anterior pituitary gland.

The authors tested 264 patients, including 32 children. A basal metabolic test was done and later was repeated two hours after the ingestion of a small protein meal consisting of the whites of three eggs, a thin slice of toast and a cup of tea. The difference between the two readings was used to denote the specific dynamic action. The average in patients having a condition diagnosed as a dysfunction of the pituitary gland was 4.47, as against 16.3 in the controls. The figure was below 10 in 86 per cent of the patients with dysfunction of the pituitary gland, against 21 per cent of the controls. This test is suggested as a valuable aid in the diagnosis of disease of the pituitary gland.

JACOBSEN, Buffalo.

GENERALIZED BLASTOMYCOSIS WITH REPORT OF A CASE IN A CHILD. CHARLES H. MCKENNA, Illinois M. J. **64**:68 (July) 1933.

McKenna, in a general review of blastomycosis preceding the report of a fatal case in a 3 year old child, points out that the disease is found among foreigners and white persons living amid insanitary conditions. The pulmonary system seems to be the most common portal of entry. The blastomycete appears in human tissues as a refractile, double-contoured, yeastlike organism which reproduces by budding. Clinically, blastomycosis presents the picture of a generalized infection, which is so much like tuberculosis that without the presence of blastomycetes in the smears it is difficult to consider any other possibility. Only one author has cited a specific case in which the patient recovered.

BARBOUR, Peoria, Ill.

CHRONIC PYURIA IN CHILDHOOD. JOHN A. BIGLER, Illinois M. J. **65**:235 (March) 1934.

The diagnosis of chronic pyuria depends on the presence of pus in the urine, the clinical symptoms, the duration of the pyuria and the findings on physical examination and on complete urologic examination. The general symptoms may be those of any chronic infection. In the older child there may be such local symptoms as dysuria, urgency, frequency and often tenderness over the bladder and kidneys. The lesions which cause the chronic infection can be divided into two groups: nonobstructive lesions and those with obstruction and urinary stasis. In either type Bacillus coli, the pyogenic organisms or, rarely, tubercle bacilli are usually present in the urine. Most of the obstructive lesions in children are congenital. One of the most common causes of chronic pyuria is urinary stasis due to obstruction somewhere in the urinary tract. Acquired obstructive lesions producing urinary stasis also occur, but they are less common than the congenital type.

The usual case of acute pyuria runs its course in about from four to six weeks with or without medical treatment. If after this time pyuria persists and medical treatment has been adequately carried out, Bigler believes that a urologic examination is indicated. If there have been recurrent attacks of pyuria the same holds true. If an abdominal tumor mass in the region of the bladder or kidneys accompanied by pyuria is present, no matter what its duration, a urologic study should be made immediately.

BARBOUR, Peoria, Ill.

MINOR ALLERGY: ITS DISTRIBUTION, CLINICAL ASPECTS AND SIGNIFICANCE. WARREN T. VAUGHAN, J. Allergy **5**:184 (Jan.) 1934.

A preliminary survey of 100 persons who were supposedly nonallergic showed that 61 of them had at some time experienced an allergic manifestation. These findings led to a house to house survey of the 251 inhabitants of a small community in Virginia, with an additional number from the surrounding territory, making a total of 508 persons. Major allergy was recognized in 10.8 per cent. Of the remainder, 48.1 per cent gave evidence of a minor allergic manifestation at some time in their history; 31.3 per cent gave no evidence, and in 9.8 per cent the evidence was questionable. Sensitization to food was present in 62.6

per cent of the 60 per cent showing some allergic manifestations, sensitization to inhalants in 23 per cent and contact sensitization in 14.4 per cent. Those with major allergic manifestations showed sensitization to some food with which they came in frequent contact, such as wheat, milk, eggs and potatoes. Those with minor allergic manifestations showed sensitization to foods eaten at infrequent intervals, such as cucumbers, watermelon and strawberries. The latter could recognize the offending food and avoid it, while the former needed diagnostic study. The foods caused various gastro-intestinal symptoms and, in some instances, dermal manifestations.

The author believes that the question is no longer "Why do some of the population become allergic?" but "Why are not all persons allergic at some time or other?", and that the difference between the allergic and nonallergic states is quantitative rather than qualitative. He thinks, too, that the survey substantiates the theory that the tendency of the allergic state is toward recovery, provided that contact is continued through a sufficiently long period.

HOYER, Cincinnati.

EVALUATION OF THE THEORY OF FOCAL INFECTION. E. H. HATTON, J. Am. Dent. A. **21**:463 (March) 1934.

The modern conception of focal infection is about twenty years old, and the "Quarterly Cumulative Index Medicus" indicates that there is more interest in the subject than there was in 1922. "There is no indication at the present time of any distinct tendency to limit tooth extractions, tonsillectomies, etc., in the actual treatment of arthritis and iritis," yet Hatton believes that "there is little reason to suppose that the routine removal of teeth, even pulpless teeth, as a preventive measure will offer any greater protection in the aggregate against the incidence of secondary disease than will routine tonsillectomy," and one therefore is entitled to conclude that tooth extraction is merely a resource in the treatment of the individual case and even so it has a limited value." The author does not assume "that all pulpless teeth are infected" and believes that there is good reason for the doctrine "that with proper selection pulpless teeth are well worth tolerating."

NOYES, Chicago.

PLASMA PROTEIN CHANGES AND SUSPENSION STABILITY OF THE BLOOD IN LOBAR PNEUMONIA. JOHANNES K. MOEN and HOBART A. REIMANN, J. Clin. Investigation **12**:589 (May) 1933.

The total plasma protein was found to be usually decreased during the febrile period of lobar pneumonia. The fibrinogen and globulin fractions were increased, the increase being present promptly after the onset and persisting for periods up to two months after the crisis. The increases in fibrinogen and globulin were closely correlated with increased viscosity of the plasma and decreased sedimentation time of the erythrocytes.

GUEST, Cincinnati.

THE INFLUENCE OF MINERAL METABOLISM UPON NEPHROTIC EDEMA. WILLIAM S. HOFFMAN and WILBUR E. POST, J. Clin. Investigation **12**:613 (July) 1933.

The relationship of mineral metabolism to edema was studied in four patients with nephrotic edema. During periods of edema formation and remission the sodium and chloride balance curves ran parallel to the curve of water balance. The amounts of sodium and chloride associated with excretion or retention of water approached the proportions of these elements found in blood plasma. Potassium was practically in balance at all times, except for a slight negative balance during edema formation. Observations were also made of spontaneous diuresis ocurring during an acute infection, the effects of excessive perspiration (in hot summer weather), the effects of the ingestion of potassium chloride and of ammonium chloride and of the intravenous injection of calcium gluconate.

GUEST, Cincinnati.

Immunity in Diabetes: Influence of Diabetes on the Development of Antibacterial Properties in the Blood. Russell Richardson, J. Clin. Investigation **12**:1143 (Nov.) 1933.

In the blood of diabetic patients (with or without infection), compared with blood from nondiabetic patients, there was no difference in complement activity, but the antibacterial power of the blood of diabetic patients tended to be less. Diabetic patients were less able than nondiabetic controls to form agglutinins following their inoculation with typhoid vaccine. Guest, Cincinnati.

Mucous Colitis in Infancy: Its Etiology and Treatment. Esther B. Hardisty, M. J. & Rec. **138**:54 (July 19) 1933.

The author gives many references to articles on the subject of mucous colitis and gives the following summary of her article:

1. Mucous colitis is characterized by the clinical symptoms of diarrhea, either continuous or intermittent, and is to a marked extent manifested by the same conditions that obtain in enteritis, dysentery, the summer diarrheas of infancy and similar conditions.

2. The etiologic factor is quoted as being Flexner's mannite nonfermenting bacillus and, in many instances, Bacillus dysenteriae Sonne. A brief discussion of these two infective agencies is given. Milk was shown to be the predominating factor in an epidemic in St. Andrews, Scotland, and in epidemics in Canada, the United States and other countries.

3. Acid-forming sugar is discussed as the causative agent from the chemical point of view. Dietotherapy is discussed as a treatment of choice, stress being laid on the importance of food relatively low in fat.

4. Dried milk low in fat is reported as being of great use in the treatment of this condition.

5. Reports describing successful treatment with dryco conclude the paper.

Williamson, New Orleans.

Epidemic Pleurodynia. N. L. Crone and E. M. Chapman, New England J. Med. **209**:1007 (Nov. 16) 1933.

The observation of thirty cases of an unusual syndrome characterized by the sudden onset, in young people, of a high fever and severe pain in the lower part of the chest or in the abdomen suggests that the "devil's grip," which was described in 1888 by Dabney in Virginia, made its appearance in Massachusetts in 1933.

Between August 1 and 25 thirty cases of this summer malady were seen in the Massachusetts General Hospital. The patients came from scattered areas in and around Boston. The age at incidence ranged from 2 to 43 years; most of the group were between the ages of 10 and 25 years, only three being younger and three older. The sexes were equally affected.

Pain is the outstanding feature, and this is usually over the lower part of the chest, the precordia or the abdomen; it occurs more often on the right side, but sometimes on the left and occasionally bilaterally. When the patients were first seen the average temperature was from 102 to 103 F. by mouth. In cases with a single episode this returned to normal within twelve hours, but in those with recurrent attacks the chart was irregular, with subsequent peaks at twenty-four and forty-eight hour intervals.

Laboratory examinations showed normal urine in each case; the white blood count was normal in all but three cases. Fluoroscopic examination and roentgenograms of the chest in fifteen cases showed no evidence of disease, and the diaphragms moved equally well. Blood cultures, the Hinton reaction and the Widal and heterophil antibody agglutinations during the febrile period were normal in six cases.

The greatest difficulty lay in deciding that the patient did not have an acute abdominal disease requiring surgical intervention. In two cases in which a diagnosis of acute appendicitis was made preoperatively exploratory laparotomy was done, but a normal appendix was removed in each. In a third patient a perforated duodenal ulcer was suspected, but exploration showed a normal abdomen. Dry pleurisy appeared later in two patients although repeated examination failed to reveal any pleuritis in the other cases.

GENGENBACH, Denver.

THE PROGNOSIS OF DIABETES IN CHILDHOOD. PRISCILLA WHITE, New York State J. Med. **33**:1 (Jan. 1) 1933.

A survey is made of 750 juvenile patients treated in Dr. Joslen's clinic from 1898 to October 1931. Of these, 217 had died, and 533 were living. Seventy-six children have survived ten years of the disease. Heredity is a great factor. Forty per cent of the entire series and 53 per cent of those who survived ten years have hereditary or familial diabetes. The effect of heredity is more evident in the younger children. The union of persons with diabetes or with those having a diabetic taint is unwise. The child with diabetes represents pure diabetes and does not show the background of obesity, disease of the gallbladder or disease of the thyroid gland, as does the adult. Trauma is not a factor, and infections play little part.

While rising hyperglycemia during fasting may occur as the child's age increases, this does not mean that the disease is progressive, but rather that the growth of body mass has brought about this change. Retardation of growth does not occur unless starvation has been permitted. Sexual maturity of children with diabetes is assured.

When from 25 to 50 per cent of the calories are given in the form of carbohydrates, from 10 to 20 per cent in protein and from 25 to 60 per cent in fat, children have developed normally. The incidence of coma is higher than in adults, because of the lapses in dietary control and because of greater susceptibility to minor infections.

Arteriosclerosis has been demonstrated in 30 cases of this group; cataracts occurred in 15. It is estimated that there are 10,000 children with diabetes in the United States, and about 1,000 new cases are found yearly. "With insulin the death rate from diabetes in children has fallen to the vanishing point."

AIKMAN, Rochester, N. Y.

EMPYEMA AS IT APPEARS TO THE INTERNIST. JOHN J. ROONEY, New York State J. Med. **33**:143 (Feb. 1) 1933.

The author reviews the clinical picture of empyema.

AIKMAN, Rochester, N. Y.

THYMIC DISEASE. E. D. CRUTCHFIELD, Texas State J. Med. **29**:318 (Sept.) 1933.

Crutchfield makes the observation that the status of the value of roentgenography in diagnosing the condition of an enlarged thymus is rather indefinite, because there is no standard of normal dimensions commensurate with the symptoms. Some thymus glands are large, yet no symptoms are present which are associated with dysfunction of the thymus gland, while other patients having only slightly enlarged glands may be expressing accentuated symptoms. The etiologic elements and mechanical relations explaining the mechanisms of this dysfunction are not considered. A series of eleven observations was made on patients in whom thymic enlargement was observed and symptoms such as cyanosis, coughing, spasms, holding of the breath or syncope were present. The technic followed was a four minute exposure, only the gastro-intestinal tract and thyroid gland being shielded. A 3 mm. aluminum filter was used. An average of two and five-tenths exposures was required, in contrast to from four to six exposures required by other technics.

The new technic resulted in amelioration of symptoms in seventy-two hours or less. Cyanosis and holding of the breath were the most common symptoms.

Results were good in every case in which no other pathologic condition was present. Nine patients showed immediate amelioration of symptoms and an uneventful recovery. One of the other patients evidenced a generalized lymphadenopathy and did not respond. The other patient not responding was subsequently considered to have epilepsy.

Crutchfield concludes that noncomplicated cases of the thymic syndrome are amenable to roentgen therapy. He believes further that the technic of large area irradiation results in fewer treatments being required and in a more prompt response to the therapy, and may possibly be a factor of importance. He believes that roentgen irradiation over the thymic area in conditions associated with some of the symptoms described and in connection with an enlarged thymic shadow has a definite place in medicine.

MOORE, Dallas, Texas.

THE TREATMENT OF FOOD ALLERGY IN YOUNG INFANTS. DAVID GREER, Texas State J. Med. **29**:370 (Oct.) 1933.

Food allergy in young infants is the paramount difficulty in modern infant feeding, according to Greer. The problem is usually that of an anatomically perfect infant, born without difficulty of a healthy mother, who exhibits one or more of the gastro-intestinal disturbances that may be encountered in young infants following the ingestion of food mixtures which, according to present knowledge of infant feeding, are in every way correct for the average baby. Among the numerous symptom complexes commonly encountered are enterospasm with persistent abdominal pain, pylorospasm, general hypertonia, cardiospasm and acute intestinal disorders with or without diarrhea. Greer points out that ordinarily any one of these conditions responds satisfactorily to dietary and medicinal measures, but not when there is an offending allergen present.

He mentions the possibility of worth-while prophylactic treatment of the unborn baby by having the mother abstain from any food to which she herself is sensitive.

The problem should be worked out systematically. First, a history of manifestations of food allergy in the parents should be obtained and foods to which they are sensitive should be excluded from the baby's dietary. Second, a complete chronological record of the infant's diet since birth and the associated digestive difficulties should be obtained. The offending food may often be apprehended in this way. Third, skin tests are justifiable, but are rarely necessary. Fourth, if no reliable indications are gained from this investigation, one may eliminate all food that the baby has been given and construct a diet of foods as completely unrelated as possible. Fifth, cow's milk is perhaps most often the offending allergen. Superheating or acidifying the milk or using it in an evaporated or powdered form often suffices to eliminate the allergic factor, and the milk may then be tolerated. But it may often have to be abandoned. The author has used with success some of the proprietary milks. He also uses corn grits as a routine in all nonallergic diets. Canned fruit juices may be substituted for fresh fruit juices, as infants are not uncommonly sensitive to the fresh fruit juices. Allergic reactions to vegetables are relatively uncommon.

Ultraviolet therapy, vigorous doses of vitamins A and D, and calcium and the administration of thyroid extract, etc., have given Greer, little, if any, assistance in treating children with food allergy. Such benefits as may be derived are too slowly attained to be of much practical value.

MOORE, Dallas, Tex.

UPPER RESPIRATORY INFECTIONS IN CHILDREN. G. H. FELLMAN, Wisconsin M. J. **32**:746 (Nov.) 1933.

Infections of the throat or of the upper respiratory tract in children are considered as a clinical entity with a definite symptomatology and with the highest incidence in March and April. During recurring epidemics they often constitute

90 per cent of the pediatrician's cases. Records of nine hundred and thirty cases showed 34 per cent of the patients to be under 2 years of age and 50 per cent under 5 years of age. There are two groups of symptoms: one of a marked and abrupt symptomatology, the other consisting mostly of anorexia, a stuffy nose and cough which is worse when the patient reclines. Abdominal pain which is sometimes difficult to distinguish from appendicitis is frequent, while sore throat is rarely mentioned, even in the presence of severe inflammation. Thoroughness in examining the throat is important—a throat that may be only moderately red at the height of the symptoms may be beefy during convalescence. Diarrhea is a usual initial symptom in some epidemics. The blood count is extremely variable. Serious complications with tragic results must be considered a possibility with even the mildest infection of the throat. The main complications in the cases studied were otitis media, in 17.5 per cent; diarrhea, in 9 per cent, and pneumonia, in 6 per cent.

JANNEY, Wauwatosa, Wis.

SUBLINGUAL ULCER: WITH SPECIAL REFERENCE TO RIGA'S DISEASE. ALAN MONCRIEFF, Brit. J. Child. Dis. **30**:268 (Oct.-Dec.) 1933.

Sublingual ulcers, apart from those in whooping cough, are rare in children.

Moncrieff reports the case of a 6 month old infant with a sublingual ulcer at the midline measuring 1 by 2 cm. The two lower incisors had erupted. No glandular enlargement in the neck could be detected. A diagnosis of a traumatic ulcer was made. When the patient was put on a mixed diet fed from a cup with a spoon the ulcer disappeared within ten days.

A condition which has been variously described as Riga's disease, sublingual granuloma and sublingual fibroma or papilloma is discussed. Histologic studies suggested that the ulcer is of inflammatory origin, with the production of excessive granulation tissue in many cases. The mechanical origin from trauma caused by teeth in well nourished babies, especially in those whose tongues are constantly "hanging out," is the most popular theory. Other theories are discussed.

LANGMANN, New York.

A PECULIAR FORM OF PURPURA. A. PINEY, Brit. J. Dermat. **45**:309 (July) 1933.

A case is reported of a youth, aged 17, who after a sudden attack of gastrointestinal disturbance presented a peculiar eruption of purpuric spots and vesicles in crops, each exacerbation being associated with a peculiarly strong fecal exhalation from the skin. Well marked monocytosis was present in the blood in the early stages of the disease. There was albuminuria late in the course, after the fever subsided. In spite of the collapsed condition of the patient at the time of admission to the hospital there was complete recovery. A plate illustrating the lesions on the right hand and foot accompanies the article.

WIEN, Chicago. [ARCH. DERMAT. & SYPH.]

HEMOPHILIA. E. T. FREEMAN, Irish J. M. Sc., March, 1933, p. 122.

The article deals with five phases: historical data, bleeding, transmission, coagulation and treatment. With regard to the latter, ovarian extracts were used. In seven of thirty-five cases it was possible to reduce the clotting time to normal, with a reduction in the severity and frequency of bleeding and a marked improvement in health. Hemorrhages occurred in the patients under treatment in spite of a good response. The author believes that the work must be carried on for a long time before any definite conclusion may be reached.

SNELLING, Toronto, Canada.

MEGALODACTYLY? CAUSE. E. C. WARNER, Proc. Roy. Soc. Med. **26**:1373 (Aug.) 1933.

A boy, aged 11 years, stated that his fingers and toes had been growing large ever since he could remember. He complained that in the winter the digits involved became very cold and blue, and cutaneous sores occurred. There was no familial

tendency to gout. The blood uric acid was 3.5 mg. per hundred cubic centimeters. The Wassermann reaction was negative. The enlargement appeared to involve especially the nonepiphyseal ends of the bones. A photograph of one hand and a roentgenogram of the same hand are given in the report.

WILLIAMSON, New Orleans.

ANAEMIA WITH LEUCOCYTOSIS AND HIGH PERCENTAGE OF EOSINOPHILS? SYPHILITIC PSEUDO-LEUKAEMIA? EOSINOPHILIC LEUKAEMIA? FRANCES BRAID, Proc. Roy. Soc. Med. **26**:1541 (Oct.) 1933.

A boy, aged 2½ years, was well developed and well nourished, but obviously anemic and of a lemon-yellow color. The liver, spleen and lymph glands were not enlarged. The Wassermann reaction of both the mother and the child was weakly positive. The blood count varied; the red blood cells numbered from 4,300,000 to 4,800,000, with hemoglobin from 48 to 74 per cent; the white blood cells numbered from 13,350 to 22,900, with from 12 to 31 eosinophils. A similar type of anemia has been attributed by some authorities to congenital syphilis. The general condition of the child was much better than one would find in either leukemia or Hodgkin's disease.

WILLIAMSON, New Orleans.

RENAL RICKETS WITH CALCIFICATION IN THE KIDNEYS. NORMAN B. CAPON, Proc. Roy. Soc. Med. **27**:408 (Feb.) 1934.

A case of this condition in a girl of 11 years is reported. Her complaints were of thirst and polyuria for about six years, headaches and shooting pains in the limbs for one year and inability to walk for nine months.

She weighed 35 pounds (15.9 Kg.) and was 40 inches (101.6 cm.) tall. Slight scoliosis, pigeon breast and genu valgum were present. The results of examination of the urine, blood and feces are given in the report.

Roentgen examination of the kidneys showed calcareous deposits in the calices of both kidneys, the pelves and both ureters. Iopax was given on two occasions. A large amount of dye was seen in the bladder, but there was none in the kidneys or ureters. Osseous changes at the diaphyses suggested renal rickets. There was delayed ossification of the epiphyses and of the carpus. The bones were smaller and more translucent than those of a healthy child of the same age. The skull was normal. There were fractures in the middle third of both fibulae and at the junction of the upper and middle third of the ulna of both arms.

WILLIAMSON, New Orleans.

TWO CASES OF CHRONIC PYURIA TREATED WITH AUTOGENOUS VACCINES. BERNARD SCHLESINGER, Proc. Roy. Soc. Med. **27**:411 (Feb.) 1934.

A girl of 9 years had suffered intermittently for more than one year from chronic pyelitis with bouts of high fever. A culture of the urine first showed Bacillus coli and later Bacillus proteus. Investigations by cystoscopy, iopax and roentgenography showed no structural abnormality of the renal tract. Calculus and tuberculosis were excluded. After all the known treatments had been tried an autogenous vaccine made from Bacillus proteus-vulgaris was given weekly for eight months, with complete recovery from all the symptoms. Cultures of the urine did not become sterile, but B. proteus was replaced by B. coli.

The second case reported was that of a girl, aged 10 years. She had suffered for three years from repeated attacks of pyuria, with severe headaches, vomiting and high fever. Roentgen examination following the intravenous injection of uroselectan revealed four ureters. A pyelogram showed four pelves, four ureters and four openings into the bladder. An autogenous B. coli vaccine was prepared and given at weekly intervals for nine months. Local and general reactions were encountered, which lasted for about twenty-four hours. The urine finally became

sterile, and pus disappeared. The general condition greatly improved, and at the time of the report the child had been free from symptoms for nine months.

WILLIAMSON, New Orleans.

WILMS' TUMOR, OR RENAL EMBRYOMA IN INFANCY. DONALD PATERSON, Proc. Roy. Soc. Med. **27**:414 (Feb.) 1934.

A case of this condition was reported in a girl of 2 years, who was admitted because of recurrent attacks of discoloration of the urine. A large mass was present in the region of the right kidney. The urine contained albumin and many pus cells, but no blood. The blood urea was 30 mg. per hundred cubic centimeters. Roentgen examination following the injection of iopax showed that the left kidney was normal. The right kidney showed no filling, which was suggestive of sarcoma. The right kidney and the large tumor were removed three days later.

Pathologists reported that the tumor showed microscopically congenital renal teratoma of Wilms (a typical rhabdomyosarcoma). The child made an uneventful recovery and was discharged from the hospital eighteen days after the operation.

WILLIAMSON, New Orleans.

EARLY EPITHELIOMA IN A CHILD AGED FOUR YEARS. J. E. WIGLEY and I. MUENDE, Proc. Roy. Soc. Med. **27**:586 (March) 1934.

A raised warty tumor the size of a split pea which, from its hard appearance, suggested a verruca necrogenica, was found on the radial aspect of the right wrist. There was also a hard painless gland palpable in the axilla, which disappeared. Otherwise the child was in perfect health. Histologic examination strongly suggested an early malignant squamous cell change. The full histologic report and a photograph of a section of skin accompany the report of the case.

WILLIAMSON, New Orleans.

IDIOPATHIC HYPERTROPHY OF THE HEART. J. C. POMPE, Ann. d'anat. path. **10**:23, 1933.

A case of idiopathic hypertrophy of the heart in a girl 7 months old is described. The heart weighed 190 Gm. (normal, 36 Gm.). Histologic examination revealed marked infiltration of the cardiac muscle fibers by glycogen. In addition, almost every other organ in the body was also infiltrated by glycogen. The literature on idiopathic hypertrophy of the heart is reviewed, and to the various theories of the etiology another is added, namely, that the condition springs from a disturbance of glycogen metabolism. Seven cases recorded in the literature were similar histologically, but glycogen was demonstrated in only a few.

MELNICK, Chicago. [ARCH. PATH.]

THE SYNDROME OF THE BLUE SCLERA: RELATION TO PARATHYROID OSTEOSIS. H. VIALLEFONT, Ann. d'ocul. **170**:289 (April) 1933.

Viallefont concludes that the most evident symptom in this syndrome is the blue color of the sclera. He suggests the importance of parathyroid dysfunction and, in certain cases, the surgical exploration of the parathyroid glands. He is of the opinion that treatment of the parathyroid glands by irradiation does not produce a complete cure, but that it improves the condition of the bones and prevents new fractures.

BERENS, New York. [ARCH. NEUROL. & PSYCHIAT.]

A STUDY OF THE LAURENCE-BIEDL SYNDROME. G. WEILL and PAYEUR, Ann. d'ocul. **171**:173 (Feb.) 1934.

Weill and Payeur report a case of the Laurence-Biedl syndrome in an infant with polydactylism, hyperfunction of the anterior lobe of the hypophysis, heredo-

syphilitic chorioretinitis and a salt and pepper appearance of the fundus. The Bordet-Wassermann reaction was positive. The authors believe that the retinitis pigmentosa in this case is without doubt of heredosyphilitic origin.

BERENS, New York. [ARCH. NEUROL. & PSYCHIAT.]

PRIMARY EPITHELIOMAS OF THE LIVER IN CHILDHOOD. P. DUCAS and G. ALBOT, Arch. de méd. d. enf. **36**:595 (Oct.) 1933.

Although relatively rare, a considerable number of primary epitheliomas have been reported. The authors were able to find sixty-nine authentic cases in the literature. The patients ranged in age from 1 month to 14 years. Contrary to former opinion, observers are now agreed that this type of neoplasm has a manifest predominance over the sarcomatous forms.

A case is reported of a male infant, 15 months of age, admitted to the Hérold Hospital in Paris with a history of progressive abdominal distention for several months previous to admission; he was also found to have chickenpox, and a careful study was made during his isolation. It was determined that the first sign of abdominal tumor appeared at the age of 10 months, and that its development for the first few months was unaccompanied by pain or by manifestations of indigestion. In addition to the enormous bilobed mass, one portion occupying the left flank down to the level of the umbilicus and the other filling the right side of the hypochondrium and extending to the crest of the ilium, there was the usual syndrome of a malignant process. Death occurred on the tenth day after admission, and histologic examination of the new growth confirmed the diagnosis of hepatic epithelioma.

AMESSE, Denver.

THE BILIARY SALTS IN THE TREATMENT OF PURULENT PNEUMOCOCCIC PLEURISY. MIHAIL CAMNER, Bull. Soc. de pédiat. de Iasi **4**:93 (Oct.-Dec.) 1933.

Excellent results were obtained by the use of bile salts in the treatment of pneumococcic empyema in children. After withdrawal of as much pus as could be obtained, a 10 per cent solution of bile salts in a physiologic solution of sodium chloride was injected into the pleural cavity. Camner used from 1 to 2 Gm. of bile salts for each injection in infants and from 2 to 4 Gm. in older children. This procedure was repeated every day or two until the aspirated pus was sterile on culture; then aspiration alone was done until no further pus could be obtained. No toxic effects were seen at any time from the use of such doses of bile salts.

LEMASTER, Evanston, Ill.

PULMONARY ABSCESS CAUSED BY INHALATION OF A HEAD OF WHEAT. A. POLAC, Bull. Soc. de pédiat. de Iasi **4**:99 (Oct.-Dec.) 1933.

A 7 year old boy aspirated a head of wheat into the right bronchus. Severe coughing and attacks of suffocation followed. Several days later, fever and hemoptysis began. A roentgenogram of the chest showed consolidation in the lower part of the right lung. A diagnosis of pulmonary abscess was made, and the abscess drained through the resected portion of a rib. The child's condition remained critical until he brought up the wheat during an attack of vomiting. Improvement was then rapid, but roentgenograms of the chest continued to show the same area of density in the right lung.

LEMASTER, Evanston, Ill.

A CASE OF FROIN'S SYNDROME. L. BALLIF and I. LUNEVSKY, Bull. Soc. de pédiat. de Iasi **4**:107 (Oct.-Dec.) 1933.

A 7 year old boy showed bizarre neurologic findings on physical examination and typical Froin's syndrome on examination of the spinal fluid. Observations at autopsy revealed extensive syringomyelia and gliomatous infiltration throughout the central nervous system. Several photomicrographs of the nerve lesions are reproduced.

LEMASTER, Evanston, Ill.

TUMOR OF THE LUNG. H. GRENET, P. ISAAC-GEORGES and L. LOUVET, Bull. Soc. de pédiat. de Paris **31**:29 (Jan.) 1933.

In a girl of 10 years a roentgenogram of the chest showed a homogeneous round shadow at the apex of the right lung. There was some impairment of resonance over this area. The child had a slight cough and some vague pain in the chest. The Wassermann reaction of the blood and the tuberculin reaction were negative. An interesting point is the persistence of this circumscribed shadow for more than five years without any change. It was thought to be due to a hydatid cyst when first seen five years ago. At the time of writing it was believed to represent a benign neoplasm, such as a neurofibroma or, possibly, a dermoid cyst of the mediastinum. In view of the patient's normal development and the absence of symptoms, it was deemed advisable to allow her to be observed further without any immediate treatment.

BENJAMIN, Montreal, Canada.

TYPHOIDAL SYNDROME WITH PNEUMOCOCCEMIA WITHOUT LOCALIZATION IN THE LUNGS. M. ARMAND-DELILLE, H. GAVOIS and P. BOYÉ, Bull. Soc. de pédiat. de Paris **31**:35 (Jan.) 1933.

A boy, aged 7 years, was brought to the hospital with a high temperature and marked toxemia. A blood culture yielded pneumococci, which were not typed. A roentgenogram of the chest failed to reveal any area of consolidation, and physical examination of the chest gave negative results, except for scattered râles on both sides. The patient had a high temperature for eight days, the temperature returning to normal gradually during the following five days. The leukocyte count was 7,920, of which only 42 per cent were polymorphonuclears. A sister of this patient, aged 11 years, was admitted to the hospital the same day with abdominal symptoms and signs of typhoid fever. A blood culture was negative, and she had leukopenia. Her temperature gradually returned to normal by the seventeenth day, but it rose again on the twentieth day and oscillated remittently for another two weeks (apparently there was a relapse). Both children showed branny desquamation a few weeks after the onset of illness. The etiology in both cases is believed to be a typhoidal infection, the exact nature of which was not determined.

BENJAMIN, Montreal, Canada.

PULMONARY ABSCESS IN A CHILD TWO AND A HALF YEARS OLD; SPONTANEOUS CURE AFTER REPEATED VOMITING. R. POINSO and J. CAPUS, Bull. Soc. de pédiat. de Paris **31**:39 (Jan.) 1933.

A boy, 2½ years old, had a pulmonary abscess following pneumonia. He spat up thick pus which contained pneumococci repeatedly. Roentgenograms of the chest confirmed the diagnosis of pulmonary abscess. A child of this age does not expectorate, and so it is thought that he vomited the pus. When he was examined two months later fluoroscopically the chest was clear. It is emphasized that cases of this nature are not very uncommon.

BENJAMIN, Montreal, Canada.

CHRONIC DEFORMING ARTHRITIS WITH SYMMETRICAL SWELLINGS OF THE FINGERS IN A CHILD TWENTY-EIGHT MONTHS OLD. M. CASSOUTE, POINSO and CAPUS, Bull. Soc. de pédiat. de Paris **31**:58 (Jan.) 1933.

A boy, 28 months old, had flexion deformities of the hips and knees, with thickening about these joints. There was also some swelling about the hands and feet, the fingers of the hands presenting an appearance resembling spina ventosa deformities. The axillary and epitrochlear glands were enlarged. The spleen was palpable. Roentgen examination showed no changes in the articular surfaces of the bones and only slight thickening of the periosteum in some bones. The Wassermann reaction of the blood and spinal fluid was negative. The blood sugar, nitrogen, calcium and cholesterol determinations were normal. There was

leukopenia with slight lymphocytosis. The condition began to develop at the age of 20 months, after a febrile period of about two months. It was therefore thought that the multiple arthritis was due to some unknown chronic infection. The only other possible etiologic factor considered was syphilis; despite the negative serologic reactions antisyphilitic treatment was given, and this was followed by some improvement. It was also planned to apply traction to the lower extremities in an effort to obtain further improvement. A photograph of the patient is reproduced to illustrate the marked deformities.

BENJAMIN, Montreal, Canada.

INFLUENCE OF INTERCURRENT INFECTIOUS DISEASES ON THE COURSE OF KALA-AZAR. P. GIRAUD and R. POINSO, Bull. Soc. de pédiat. de Paris **31**:113 (Feb. 21) 1933.

In eleven of twenty-three cases of kala-azar intercurrent infections were followed by improvement in the course of the disease. When an intercurrent infection developed during the initial period of the disease the signs of kala-azar seemed to be hastened in their appearance; when such an infection occurred during the course of well established kala-azar, some improvement followed at times, whereas the condition was aggravated at other times. The latter was especially true when the patient was already weakened by the disease. For this reason it is thought that patients who have suffered from kala-azar for a long time should not be hospitalized, to avoid subjecting them to the possibility of contracting some intercurrent infection which they might not survive. It was believed that the presence of high fever might explain the marked improvement noted in some cases following an intercurrent infection. With this in mind, ten injections of an arsenical preparation (oxyacetyl aminophenylarsinic acid diethylamine) were given to a child with antimony-resistant kala-azar. Each treatment was followed by marked hyperpyrexia, and marked improvement took place. To insure against relapse, a course of antimony was given after the pyretotherapy. It is suggested that this form of treatment might prove valuable in cases of antimony-resistant kala-azar.

BENJAMIN, Montreal, Canada.

ASTHMATIFORM ATTACK PROVOKED BY MECHANICAL IRRITATION OF A TONSIL (A PIECE OF A GRAIN OF OATS). P. ARMAND-DELILLE and H. GAVOIS, Bull. Soc. de pédiat. de Paris **31**:150 (March 21) 1933.

A girl, 2⅓ years old, was admitted to the hospital because of severe dyspnea of the asthmatic type. On the third day after admission a grain of oats was removed from the right tonsil. The illness ran a febrile course for ten days, although the breathing, which had become considerably improved, became normal soon after the removal of the foreign body from the tonsil. Considerable inflammatory reaction of the mucous membrane was present around it, and it is considered that an extension of this process to the tracheobronchial mucosa, as well as a reflex irritation, might account for the marked respiratory distress. Examination of the blood showed no eosinophilia.

BENJAMIN, Montreal, Canada.

PSEUDORUB OF PLEURAL FRICTION IN EMPYEMA; FIBRINOPLEURITIC RUB. MARTINEZ VARGAS, Bull. Soc. de pédiat. de Paris **31**:151 (March 21) 1933.

The author describes a "fibrinopleuritic" friction rub which he found to be present in cases of empyema. It occurs in cases in which there are large agglomerated masses of fibrin. Some of these may be very large; a photographic reproduction of one which measured 13 by 9 by 1.5 cm. is shown. Their structure is spongy, or cakelike, and pus circulates in the interspaces, producing a sound which resembles a pleural friction rub. It is an indication for immediate thoracotomy to obtain drainage of the pus as well as the masses of fibrin. In order to facilitate the complete evacuation of the latter it is recommended that portions of two ribs be resected, and that the operation not be limited to resection of a single rib.

BENJAMIN, Montreal, Canada.

GENERALIZED MYOSCLEROSIS. C. ROEDERER and J. HALLÉ, Bull. Soc. de pédiat. de Paris **31**:163 (April 25) 1933.

A girl, 5 years old, showed some limitation of movements of the neck, trunk and extremities. This appeared to be due to hardness and inability of the muscles to contract fully. The lower extremities were thin, and the feet were held widely separated, with the knees in the varus position, as can be seen in a photograph of the child which is reproduced. The hands were stiff as a result of hardening of the deep tissues of the palms, although the superficial skin appeared to be normal. Roentgenologic examination did not reveal anything of importance. The electrical response of the muscles showed no quantitative changes, but there was a definite slowness in response. It is thought that this case does not fit into the classifications of myositis ossificans or scleroderma, and the name myosclerosis is suggested.

BENJAMIN, Montreal, Canada.

INTESTINAL PARASITES IN CHILDREN IN THE VICINITY OF PARIS. P. NOBÉCOURT, C. BIDOT and A. COMNINOS, Bull. Soc. de pédiat. de Paris **31**:170 (April 25) 1933.

Of 300 children of all ages, 154, i. e., 51.3 per cent, showed ova of intestinal parasites in the stools. The incidence of intestinal parasites was rare in infants under 1 year of age and increased steadily in children from 2 to 16 years old. Blood smears from 21 children with parasites showed that 23 per cent had eosinophilia of from 5 to 12 per cent; in 15 children without parasites examination of the blood revealed eosinophilia in 33 per cent, the highest being 9 per cent. The sexes were about evenly afflicted, with a slight preponderance in the girls. Digestive disorders were frequently accompanied by the presence of intestinal parasites in the stools of children over 2 years old. In infants with digestive disorders ova were rarely present in the stools.

BENJAMIN, Montreal, Canada.

INTRAMUSCULAR INJECTIONS OF OUABAIN IN TOXIC COLLAPSE AND IN BRONCHOPNEUMONIA IN INFANTS. JEAN CATHALA and ALBERT NETTER, Bull. Soc. de pédiat. de Paris **31**:177 (April 25) 1933.

Intramuscular injections of from 0.125 to 0.25 mg. of ouabain in infants with bronchopneumonia, especially following whooping cough, are said to be of distinct value. This treatment is also advised in toxic infections of the upper respiratory tract in small infants, when circulatory collapse becomes imminent and pulmonary edema develops.

BENJAMIN, Montreal, Canada.

ARREST OF PULMONARY EMBOLIC GANGRENE. J. HALLÉ and ODINET, Bull. Soc. de pédiat. de Paris **31**:181 (April 25) 1933.

A boy, 10 years old, was operated on for umbilical hernia. Five days later he was seized with severe pain in the left side of the chest, which was followed somewhat later by a similar pain on the right side. It was believed that these pains were due to pulmonary emboli. Fifteen days later a fetid odor of the breath was noticed, and one week later he expectorated a small quantity of extremely fetid material after an attack of coughing. There was no more expectoration after that, and the boy made continued improvement until he was completely cured. He received subcutaneous injections of antigangrenous serum, as well as a number of other medications and local applications to the chest. Hallé and Odinet speak of the condition as an arrest of the gangrenous process, because they believe that in many such instances a flareup of the pathologic process may occur later.

BENJAMIN, Montreal, Canada.

Cyst of the Great Omentum in a Child Four Years Old. L. Guillemot and Jacques Leveuf, Bull. Soc. de pédiat. de Paris **31**:190 (April 25) 1933.

A boy, 4 years old, was brought to the hospital because of repeated attacks of vague abdominal pain accompanied by progressive enlargement of the abdomen for about a year previously. There was never any vomiting, and the stools were normal. At operation a large cyst of the great omentum was easily removed, and two tiny cysts, which were free in the peritoneal cavity, were also removed. Histologically, the tumors were diagnosed as cystic lymphangiomas. It is pointed out that although the condition was found in a boy in this particular instance, it is much more frequently encountered in girls. Surgical extirpation is usually easily and successfully performed and is not followed by any recurrence of the condition.

Benjamin, Montreal, Canada.

Cystic Lymphangioma of the Base of the Neck with Intrathoracic Prolongation Outlined by Roentgenography. A. Martin, M. Lelong and J. Odinet, Bull. Soc. de pédiat. de Paris **31**:210 (May 16) 1933.

A girl, just under 3 years old, presented a cystic swelling about the size of a hen's egg in the left supraclavicular fossa. Roentgenologic examination demonstrated that the swelling extended into the thorax. With expiration the thoracic part became much smaller and the swelling in the neck enlarged. The tumor may be observed for a time without any radical treatment or excised surgically or treated by the roentgen rays.

Benjamin, Montreal, Canada.

Lymphangioma of the Neck. A. Martin and M. Lelong, Bull. Soc. de pédiat. de Paris **31**:212 (May 16) 1933.

A girl had a lymphangioma at the base of the neck on the left side, which extended retrosternally for a short distance. The sac was ruptured at operation, and a thin chocolate-colored fluid was released. About 2 cm. of the sac had to be left out of the excision, as it was adherent to the external aspect of the internal jugular vein. This area was painted with a solution of zinc chloride. The child made a good recovery.

Benjamin, Montreal, Canada.

A Case of Still's Disease. J. Flarand, R. Broca and Gilbrin, Bull. Soc. de pédiat. de Paris **31**:215 (May 16) 1933.

An Armenian girl, 5½ years old, presented a typical picture of Still's disease. At the age of 2½ years she had multiple arthritis, which lasted about two months. There was a long period of freedom from symptoms. A second onset of arthritic symptoms was noted at about 5 years of age, and she had become steadily worse since then. As is usual in this disease, roentgenologic examination of the bones showed no pathologic changes.

Benjamin, Montreal Canada.

Sarcoma of the Mediastinum. H. Grenet, P. Isaac-Georges, L. Louvet and P. Arondel, Bull. Soc. de pédiat. de Paris **31**:218 (May 16) 1933.

Pathologic specimens of mediastinal lymphosarcoma with multiple metastases which occurred in a girl, 7 years old, were presented. The clinical course of the condition began with a hemorrhagic pleural effusion on the right side. The tumor grew rapidly, and the child died about six weeks after the onset of the symptoms.

Benjamin, Montreal, Canada.

Splenomegalic Form of Hodgkin's Disease. J. Hallé, Derome and Odinet, Bull. Soc. de pédiat. de Paris **31**:241 (May 16) 1933.

A boy, 4½ years old, was admitted to the hospital because of enlargement of the spleen. He had an enlarged left submaxillary lymph node, which varied in size from time to time during the two years prior to admission. No other adenopathy was found. He had lost weight and was considerably anemic. After a

few weeks several small glands appeared in the right supraclavicular fossa. Hodgkin's disease was then diagnosed, and this diagnosis was confirmed by biopsy on one of these glands. He died a few weeks later.

BENJAMIN, Montreal, Canada.

THE NORMAL OSSIFICATION AND PATHOLOGIC MANIFESTATIONS OF THE ANTERIOR TUBEROSITY OF THE TIBIA. ADOLPHE PERROT, Rev. d'orthop. **20**:498 (Sept.-Oct.) 1933.

There has been considerable divergence of opinion concerning the normal ossification of the anterior tuberosity of the tibia. The present paper is a résumé of the various opinions and a study of the question from the roentgenologic and postmortem aspects. The author believes that ossification does not proceed from the apophysis alone, but is a combination of ossification proceeding from both the apophysis and the epiphysis. This ossification commences at about the age of 10 years and is usually complete at about the age of 14 years. The number of points of ossification may vary, not only in various children, but in the two tibias of the same child. At the beginning of ossification there is considerable space between the centers of ossification and the anterior border of the tibia. As ossification proceeds this space diminishes, and when ossification is complete, little or no space remains. Occasionally this space does not close completely and may be seen in roentgenograms of adults.

With reference to Osgood-Schlatter disease, the author has not seen evidence of inflammation, necrosis or endarteritis obliterans in pathologic sections taken from the site of the lesion. Culture of specimens has given negative results. Perrot would term such a lesion an *"apophysiolyse."* RYAN, Vancouver, B. C.

PSOITIS SECONDARY TO A RARE FOCUS AND WITH UNCOMMON SYMPTOMATOLOGY. VANNUCCI and DI CUNTO, Rev. d'orthop. **21**:336 (July) 1934.

A boy, 10 years of age, was admitted to the hospital on Nov. 20, 1933, with a condition which had been diagnosed as primary psoitis. Two weeks previously he had taken a cold bath, following which he limped. Pain radiated down the thigh to the knee, and spasm of the muscles occurred with the slightest movement of the hip joint. The boy had been in good health previously. The father stated that he did not have a thermometer, but did not think that the boy had had an elevation of temperature at any time. On admission the thigh was flexed. There was slight atrophy of the muscles on the right side; all the movements of the knee were free. Passive movement of the hip produced pain and spasm of the muscles. There was no free movement of the hip. Percussion over the iliac spine produced a dull ache. On palpation of the abdomen an ovoid mass was felt lying near the inner side of the ilium, deep down. The mass was orange-sized, firm and somewhat irregular in outline. The regional lymphatic nodes were enlarged. The Pirquet reaction was negative. Roentgenograms of the lumbar spine, the pelvis and the femurs showed no abnormality. The urine was normal. During the stay in the hospital there was no elevation in the temperature. On December 2, an exploratory operation was performed, and a mass was found attached to the iliac wall about 6 cm. below the crest. Pus was evacuated. The wound drained for two days, after which no further disorders were noted. Culture of the pus revealed Staphylococcus aureus. The points of special interest are: (1) the normal roentgenograms; (2) the appearance of the suppurative subperiosteal mass without fever, following an abrupt onset; (3) the peritoneal reaction without clinical signs, and (4) the rareness of primary osteoperiostitis of the ileum.

RYAN, Vancouver, Canada.

THE HAND-SCHÜLLER-CHRISTIAN SYNDROME. S. PADOVANI, Arch. di ottal. **40**:281 (June); 297 (July-Aug.) 1933.

The author reports a case presenting the characteristic picture of the Hand-Schüller-Christian syndrome. A boy, aged 7 years, had had polyuria, exophthalmos

and anomalies of dentition at the age of 4 years. The legs were cyanotic; the few remaining teeth were irregular and abnormally large, and the skull was large and tender on pressure. Exophthalmos was more marked on the left side (23 mm., Hertel). Vision with correction was ½ in the right eye and ⅛ in the left; the fields and the fundi were normal, except for slight dilatation of the retinal veins. About 7 liters of urine was passed daily. Roentgen examination showed defects in the skull, especially on the left side, where the upper, outer and lower orbital walls were almost entirely absent. The anterior and right posterior fontanels were not closed. The sella was large, and the anterior clinoid processes were eroded. As a result of the defect in the left orbital floor the left globe was displaced downward 4 mm. in comparison with the right one. The exophthalmos on this side may probably be explained as due to the pressure of the brain through the defective orbital wall.

GIFFORD, Chicago. [ARCH. OPHTH.]

INFANTILE GIGANTISM. E. TATAFIORE, Pediatria **42**:595 (June 1) 1934.

Tatafiore discusses in full infantile gigantism and presents his observations on three patients who were under his care in the outpatients' services of the Pausilipon Hospital of Naples. He describes the growth of these children as being normal in relation to the general body contour; that is, no disproportion of any particular part of the body developed, but there was a uniform overgrowth which gave the appearance of gigantism.

The author examined the patients from the clinical and hereditary points of view. He concludes that these cases represent those of true infantile gigantism, in which there are no loss of harmony in the body outlines, no tendency to obesity and no tendency pointing to the existence of diathesis.

SIGNORELLI, New Orleans.

LIPOID NEPHROSIS. F. BONIVENTO, Pediatria **42**:620 (June 1) 1934.

Bonivento presents a brief review of the latest conception of the etiology, pathogenesis, diagnosis and treatment of lipoid nephrosis, together with a description of two cases observed by himself. In one of his cases the condition represented a mixed form of nephritis and nephrosis, while the second case was one of pure lipoid nephrosis. In both cases the treatment was dietetic, being based on the administration of fruits, raw vegetables and lipoids, with remarkable improvement. In the case of mixed nephritis and nephrosis intercurrent cystitis seemed to have aided the improvement of the original condition; in the case of pure lipoid nephrosis proteinotherapy gave but slight results.

SIGNORELLI, New Orleans.

HEMORRHAGIC PLEURITIS CAUSED BY THE PARATYPHOID B BACILLUS IN A GIRL OF 4 YEARS. A. BOLLETTINO, Riv. di clin. pediat. **32**:40 (Jan.) 1934.

A case of pleuritis with hemorrhagic exudate in a girl, aged 4 years, is reported. The exudate later became purulent.

The onset of the illness was about two months previous to the effusion and was marked by abdominal pain and diarrhea. Fever had persisted, being of the remittent type. Although cultures of the fluid were negative, a positive Gruber-Widal reaction for the paratyphoid B bacillus and the history of the onset indicated that the etiologic agent was the parathypoid B bacilli. There were some bronchitis and bronchopneumonia. Tuberculin reactions were negative, and no tubercle bacilli were found in the sputum.

Treatment was by five thoracenteses. The child was reported completely cured after three months.

HIGGINS, Boston.

THE CARBOHYDRATE DIET IN PYURIA. A. WIEDERFOLD, Arch. de hosp. d. niños, Roberto del Rio **4**:74 (June) 1933.

A child 5 months old had interstitial suppurative nephritis following influenza. He recovered when fed a diet containing from 20 to 25 Gm. of carbohydrate per kilogram of body weight.

SANFORD, Chicago.

SIXTEEN CASES OF FOREIGN BODY IN THE ESOPHAGUS. J. DE ANDRADE MEDICIS, Arch. do hosp. do Centenario **1**:7 (Dec.) 1932.

Sixteen cases of foreign bodies in the esophagus are reported. Eight of the foreign bodies were coins; one was a piece of copper metal; one was a ring; three were bones, and two were sets of false teeth. The roentgen rays and esophagoscope were used to locate the object and for the operative removal of the same. The author recommends the use of instruments with which one is familiar and which one can use deftly. The operative measures are discussed in detail. Contraindications to the use of an esophagoscope include dilatation and aneurysm of the aorta.

HERRON, Spokane, Wash.

INTESTINAL AUTOINTOXICATION WITH EXTREME EMACIATION; PELVIC ADENITIS. JUAN CARLOS NAVARRO and SARA DE ALZAGA, Arch. méd. d. hosp., Buenos Aires **15**:159 (April) 1933.

One case of this condition is reported in detail. The onset was acute, with early symptoms of an acute condition of the abdomen, the abdomen being rigid, tympanitic and painful on touch. The disease was thought to be acute appendicitis, and instead of operating, medical management with the application of ice-bags to the abdomen was carried out. The pain, tenderness and fever soon disappeared, only to reappear again as suddenly as before within a few days. This picture continued for two months, during which time the child became extremely emaciated. A large abdominal tumor mass in the right lower quadrant was palpated and was found to be outside the bowel after a barium sulphate enema was given. This was thought to be due to acute pelvic adenitis following the appendicitis. The mass gradually disappeared within four months. No particular reason is given for calling this condition pelvic adenitis rather than a pelvic abscess.

HERRON, Spokane, Wash.

CERVICAL ADENOPATHY IN INFANCY. R. VALDÉZ DÍAZ, Arch. de med. inf. **2**:265 (April) 1933.

One should always think of Hodgkin's disease in chronic adenopathy of the neck. Sternberg's giant cells, which appear in sections of the ganglion, are the only basis for a positive diagnosis. The tuberculous nature of the disease is not conclusively proved. There is no specific curative treatment.

SANFORD, Chicago.

HEMOTHERAPY IN THE PULMONARY PHLEGMASIAS IN INFANCY. ENRIQUE SUÑER Y ORDÓÑEZ, Med. de los niños **35**:76 (March) 1934.

This is a report on the use of whole blood in the pneumonias of children. Small doses (from 15 to 30 cc.) were given, for the most part intramuscularly, at frequent intervals (from twenty-four to forty-eight hours), with excellent results.

DWYER, Kansas City, Mo.

ESSENTIAL THROMBOCYTOPENIA OF WERLHOF. VALDYR DE ABREU, Pediatría, Rio de Janeiro **1**:3 (Jan.) 1934.

This condition was seen in a child 9 years old. The symptoms lasted only a week. They consisted of petechiae and larger hemorrhages on the extremities. The bleeding time was twenty-seven minutes, and the number of blood plates fell to 11,200.

SANFORD, Chicago.

TWO CASES OF AGRANULOCYTOSIS IN CHILDREN. R. GANSER, Frankfurt. Ztschr. f. Path. **44**:329, 1932.

The important manifestations in these cases were hemorrhagic diathesis, enlargement of the liver and mastoiditis. Angina was present in one case. In both instances the blood showed marked reduction in the number of the red corpuscles and marked leukopenia, with relative lymphocytosis and thrombopenia. In addition, the second case revealed polychromatophilia of the red corpuscles and a moderate number of normoblasts. Several blood transfusions were given, resulting in an improvement of the blood picture. Gradually, however, the anemia and leukopenia recurred. Autopsy revealed hemorrhages into the skin, the serous and mucous membranes, the myocardium, the surface of the liver and kidneys and the subperiosteal space. In the first instance the lymph nodes in the region of the neck and hilus of the liver were moderately enlarged, while in the second case all the lymph nodes were enlarged. The mucosa covering the tonsils showed areas of hemorrhage and necrosis. The bone marrow of the femur was dark red in both instances. Histologic examination of the bone marrow revealed an almost complete disappearance of granulocytes and megakaryocytes. Erythrocytes, erythroblasts and a large number of cells that showed only a small amount of cytoplasm were present. The nuclei of the latter varied in size. These cells resembled microlymphocytes and mesolymphocytes. Also, cells apparently identical with the hemocytoblast (stem cell) of Maximow were recognized. The lymph nodes revealed microlymphocytes, mesolymphocytes and a few macrolymphocytes and hemocytoblasts. Occasionally, eosinophilic myelocytes were also seen. The spleen contained microlymphocytes and mesolymphocytes, a few plasma cells, myelocytes and many partially destroyed erythrocytes. Small and large lymphocytes were present in the liver in addition to eosinophilic myelocytes, which were abundant in the second case. In spite of the presence of many microlymphocytes and mesolymphocytes, Ganser does not believe that these two cases are characteristic of chronic (aleukemic) lymphadenosis. He believes that these cells are closely related to the hemocytoblasts and very likely are myeloid cells. It is possible that the stem cells and their derivatives are increased in number because of a pathologic irritation. Ganser concludes that severe damage, possibly combined with a constitutional factor, produces marked destruction and necrosis of the bone marrow and may be responsible for the picture of so-called panmyelophthisis. A less severe irritation may produce atrophy of the blood-forming organs. Another type of irritation, still less severe, may cause, in addition to atrophy, regenerative and compensatory blood formations in the bone marrow and other organs. He believes that the latter explanation holds for the two cases reported.

O. SAPHIR, Chicago. [ARCH. PATH.]

PARALYSIS OF A SERRATUS MUSCLE FOLLOWING SERUM SICKNESS. E. SCHILLING, Med. Klin. **29**:907 (July 1) 1933.

A man, 26 years old, was given a prophylactic injection of tetanus antitoxin in his right arm on the day following a puncture wound of his foot. Eight days after the injection typical serum sickness developed, with glandular swelling, fever, malaise and urticaria. By the fourteenth day, he was quite well, but noticed that he could not raise his right arm. Examination showed paralysis of the right serratus anterior muscle, which persisted for about six months without improvement. Complete use of the muscle returned in about eighteen months.

At the time of writing this report only one other case of paralysis following the use of tetanus antitoxin had been reported in the German literature.

DOOLEY, Kent, Conn.

INSULIN KETONURIA IN CHILDHOOD. W. SICK and M. WEICHSEL, Monatschr. f. Kinderh. **58**:383, 1933.

There is a belief that insulin relieves glycosuria in young persons with diabetes but does not affect the ketonuria. Sick and Weichsel tested this hypothesis by

giving normal children first a normal diet and then a hunger diet and injecting 15 units of insulin. In the same way they tested children with diabetes by increasing the dose of insulin. They find that insulin is not a factor in causing ketonuria, and that when such a condition exists it is the result of improper dosage.

GERSTLEY, Chicago.

CLINICAL AND EXPERIMENTAL RESEARCHES ON THE SIGNIFICANCE OF THE IRON CONTAINED IN THE FOOD: III. F. REIMANN and F. FRITSCH, Ztschr. f. klin. Med. **120**:16, 1932.

Prolonged ingestion of foods rich in iron considerably improves the blood picture in anemia sensitive to iron, and there is no essential difference in action between food iron and medicinal iron (FeCl). The iron is cleaved from the food and dissolved in the gastro-intestinal tract, chiefly by the action of gastric hydrochloric acid and enzymes, which transform from one quarter to one third of the iron in the food. Absorption then occurs. Some of the iron is excreted in the feces. The "active" iron, therefore, is slight and is decreased in such conditions as achylia gastrica.

KUGELMASS, New York.

REPORT OF TWO CASES OF FAMILIAR LIPOID NEPHROSIS. M. BUSSEL and J. SULKES, Pedjatrja polska **13**:156, 1933.

Two sisters came to the Polyclinic for Children's Diseases in Warsaw. One was 2 years and 4 months old, and the other 9 months old. The characteristic feature in these cases was that the mother was suffering from kidney trouble. Two other children in the family had died of kidney disease. Another point of interest was the early onset of the disease. The older sister became ill at the age of 9 months and the other at the age of 4 months. The condition usually becomes better or worse without any treatment.

Children with this condition are susceptible to secondary infection; for instance, in these cases the older child often has infection of the upper respiratory tract, and the younger has gastro-intestinal disturbances.

KRUPINSKI, Chicago.

DIFFERENT PHYSIOLOGIC VARIATIONS IN THE HEARTS OF CHILDREN. E. L. LEVATUS and P. D. GUREVITCH, Okhr. Zdor. Det. i Podr., no. 5-6, 1933, p. 60.

Three thousand, five hundred and ninety-six subjects, aged from 8 to 18, were studied. Of these, 500 were watched for five years. A selected group of 194 were examined five times during one year. All pathologic cases were excluded. The incidence of inorganic heart murmurs, distant heart sounds, muffled first sound, accentuated second sound and split second sound was studied. The most frequent sign was inorganic murmur, which tended to diminish with increasing age. The second most frequent sign was distant sound, which increases with age. The inorganic and functional murmurs are discussed so far as nomenclature and etiology are concerned. The authors are inclined to agree with Savetsky, Tregoubof and Feer that the production of the murmurs is due to deficiency of the mitral valve, which depends on hypertonicity and hypotonicity of the sympathetic nervous system. These authors think that the proper name for the murmur should be inorganic, to differentiate it from organic murmur, which is a pathologic condition of the valve itself. Examination of the blood showed that anemia had no relation to these murmurs. Pharmacologic study indicated that the murmurs were due to disorders of the vegetative system. The most frequent location of the murmur was at the apex. The murmur was most frequently heard when the patient was in a recumbent position. It was found that inorganic murmur persisted in 46.4 per cent of the cases during one year of observation and in 36.2 per cent throughout five years. It disappeared in 5.8 per cent within one year and in 18.7 per cent within five years. No relation could be demonstrated between infections and the inorganic murmurs, although constitutional factors, such as asthenia, seemed to have an influence.

The location of the muffled first sound was similar to that of the inorganic murmur, and this sound could change to an inorganic murmur. The fact that the muffled first sound was best heard when the subject was in a recumbent position and the lack of influence of infectious disease favored the idea that the muffled first sound was the rudimentary form of the inorganic murmur and that it represented a variation from the normal.

Distant heart sounds were heard in children of better muscular development. The increase of distant sound with age was thought to be the result of vagotonicity of the adolescent period. Distant sounds were often associated with bradycardia. Infections were not found to influence the appearance of distant sounds.

Accentuation of the second sound was found to occur in the absence of nephritis and elevation of the blood pressure. The split second sound appeared when the subject was in a recumbent position, disappeared after exercise and frequently when respiration was arrested and could not be demonstrated to be connected with infection; it was thought to be due to vegetative dystonia. Examination of psychoneurotic children and normal children showed inorganic variations of heart sound equally present in both groups.

SEMENENKO-MCKHANN, Boston.

GESSE'S CALORIMETRIC SIGN IN THE DIAGNOSIS OF RETROPERITONEAL SWELLINGS. ZAYTSEVA, Vrach. delo **16**:84, 1933.

The author discusses the value and the significance of Gesse's calorimetric sign which was first described by him in the various Russian medical journals and in the *Klinische Wochenschrift* in 1929. It consists in a variation of the cutaneous temperature of the lower extremities, depending on an irritation or paralysis of the lumbar division of the sympathetic nervous system owing to its compression by a retroperitoneal neoplastic or inflammatory mass. In the early stages of compression, or in the stage of irritation, there is a lowering of the temperature of the corresponding lower extremity with a hyperhydrosis and increased pilomotor reflexes. In the later stages of compression, which result in the paralysis of nerve branches, there is an opposite effect, namely, an increase in temperature with an anhydrosis and decreased pilomotor reflexes.

The case histories of four patients are given in which the diagnosis and the exact location of a retroperitoneal mass could be made by a barely perceptible variation in temperature (from 1 to 3 C. or from 33.8 to 37.4 F.), between the two lower extremities, before it was possible to do so by other clinical means. The diagnosis in each of the cases was confirmed either at operation or at autopsy.

The conclusions are that: 1. Gesse's calorimetric sign is a valuable aid in the diagnosis of retroperitoneal swellings. 2. It is an early sign of their growth and can be observed even when by the usual clinical means a definite diagnosis is not possible. 3. Gesse's sign allows not only the localization of the mass to the right or to the left of the peritoneal space, but also indicates the stage of its development, since in the early stages there are signs of irritation, and in the later, signs of paralysis of the compressed nerve branches.

BODER, Chicago.

THE TREATMENT OF SUPPURATIVE INFLAMMATORY PROCESSES BY THE USE OF INSULIN AND DEXTROSE. I. M. NEIMAN and E. M. TIMOFEYEVA, Vrach. delo **16**:213, 1933.

The authors report the results of their studies of the action of insulin and dextrose on the course of suppurative inflammatory processes in mice and rats. Identical suppurative wounds were produced artificially by the same methods in mice and rats, after which the animals were divided in four groups. Group I received 1 cc. of 15 per cent solution of dextrose subcutaneously four times a day. Group II received 1 cc. of 15 per cent solution of dextrose together with 0.01 unit of insulin. Group III received 0.01 unit of insulin alone four times a day. Group IV was left as a control group.

The results were as follows:

1. Group I became definitely worse after the first injection. Poorly granulating and poorly healing wounds were observed in this series. 2. Group III showed a slight slowing of the healing process as compared with the control group. 3. Group II showed marked improvement and a rapid healing of the wounds.

The conclusions are that: 1. The injection of dextrose alone has a detrimental effect on the healing of suppurative wounds. 2. The use of insulin alone causes a slight slowing of the healing process. 3. The combination of dextrose and insulin produces a marked and rapid improvement of the suppurative wounds in mice and rats.

The authors do not believe that the combination of dextrose and insulin has previously been tried in the treatment of suppurative processes either experimentally on animals or clinically.

BODER, Chicago.

CLINICAL SIGNIFICANCE OF THE MCCLURE-ALDRICH REACTION IN CHILDREN; PRELIMINARY REPORT. N. M. FRISHMAN and C. WEISBURG, Vrach. delo **16**:398, 1933.

Frishman and Weisburg report the results of their investigations on the McClure-Aldrich reaction in children. The test consists in the intradermal administration of 0.2 cc. of physiologic solution of sodium chloride and observation of the time necessary for the disappearance of the papule produced.

The experiments were conducted on a total of one hundred and thirty-six children; this group included normal children of various ages, as well as children with acute and chronic diseases. The authors designate the reaction by the letters I. D. W. R. (*intradermal Wasserreaction*) and the time of disappearance of the papule by Q. Z. (*Quadelzeit*).

The conclusions were:

1. The McClure-Aldrich reaction, though still in the experimental stage, undoubtedly possesses great clinical significance. 2. In the series of cases studied the physiologic Q. Z., or the Q. Z. in normal children, was found to be fifty minutes. regardless of the age, while in pathologic conditions it presented various fluctuations, which consisted most frequently in a shortened Q. Z. 3. In the cases in which edema was not present the location of the reaction was unimportant. On the contrary, in cases of edema, the Q. Z. was found to be considerably shortened in places where the edema was most marked. 4. The McClure-Aldrich reaction is especially valuable in the diagnosis of the so-called preedematous stage in nephritis, carditis and nutritional disorders of infants. 5. In the series of cases studied the Q. Z. was found to be shortened in the more acute or active stages of the disease, while it became prolonged with improvement of the patient. It was thus possible in many instances of acute infectious processes to judge the activity and progress of the disease by the McClure-Aldrich reaction.

BODER, Chicago.

ANEMIA IN ANCYLOSTOMA DUODENALE. M. YOSHIDA, J. Pediat. (Tokyo), Dec. 20, 1933, p. 2240.

The author used expressed juice of fresh calf's liver injected rectally to combat anemia due to Ancylostoma duodenale in an 11 year old child. Only 3 cc. of the juice was effective in restoring the hemoglobin from 7.9 Gm. per hundred cubic centimeters to 9.5 and erythrocytes from 3,900,000 to 4,530,000 within two weeks.

KATO, Chicago.

SUBPHRENIC ABSCESS IN A CHILD OF 1½ YEARS. A. Y. VAN DER MEULEN, Nederl. tijdschr. v. geneesk. **78**:278 (Jan. 20) 1934.

The author describes a case of subphrenic abscess in a child aged 1½ years, caused by a needle which probably reached the liver through the digestive tract and primarily caused abscess of the liver.

VAN CREVELD, Amsterdam, The Netherlands.

Nervous Diseases

ETIOLOGY OF EPILEPSY WITH SPECIAL REFERENCE TO ITS OCCURRENCE IN TWINS. AARON J. ROSANOFF, LEVA M. HANDY and ISABEL AVIS ROSANOFF, Arch. Neurol. & Psychiat. **31**:1165 (June) 1934.

This is the report of a study of mental disorders in twins, with special reference to epilepsy occurring in one of twins. The article is not easily summarized. The authors discuss the probable factors of epilepsy, which are heredity, trauma and lack of development.

The article should be read in its entirety. BEVERLY, Chicago.

SECOND ATTACKS OF POLIOMYELITIS. T. B. QUIGLEY, J. A. M. A. **102**:752 (March 10) 1934.

It is probable that permanent immunity is not always conferred when an infectious or contagious disease is contracted. Second attacks of scarlatina, rubeola, rubella, pertussis, parotitis, variola, varicella and typhoid fever have been reported. Fourteen cases of second attacks of poliomyelitis have been recorded, and Quigley adds another to the list. BONAR, Salt Lake City.

THE PARENT-CHILD RELATIONSHIP IN SCHIZOPHRENIA: I. OVER-PROTECTION—REJECTION. JACOB KASANIN, ELIZABETH KNIGHT and PRISCILLA SAGE, J. Nerv. & Ment. Dis. **79**:249 (March) 1934.

This personality disorder has its roots in the early childhood of the person whose life has been unusually well guarded and overprotected, often the center of emotional storms in the family. In many cases the parents were so wrapped up in their child that they hampered his development and probably interfered with his psychosexual maturity. Schizophrenics rarely, if ever, marry.

"Over-protection" includes excessive contact with the parents, prolongation of infantile care, prevention of the development of independent behavior and lack or excess of maternal control. The causes of overprotection may be: (1) a long period of anticipation and frustration in the life of the mother during which her desire for a child was thwarted by sterility or by miscarriages or deaths of infants; (2) conditions in the child that endangered his survival, physical handicaps, illnesses frightening to the mother and the like; (3) sexual incompatibility of the mother and father; (4) social isolation of the child; (5) emotional impoverishment in early life; (6) the development of dominating characteristics through the assumption of undue responsibility in childhood and continuance of this rôle in marriage, and (7) thwarted ambitions.

Forty-five unselected cases of schizophrenia were studied. In 60 per cent there was a definite history of maternal overprotection. This period of overprotection extended into the adult life of the patient and, at times, even into his life in the hospital. Many of the patients presented evidence of physical as well as emotional inferiority. JAHR, Omaha.

PATHOGENIC FACTORS IN SOME EPILEPSIES. JULES H. MASSERMAN, J. Nerv. & Ment. Dis. **79**:322 (April) 1934.

Two cases are reported from the Baltimore Psychopathic Hospital. In each there was a history of epileptic attacks or symptoms leading to these attacks beginning in childhood. In each the epilepsy was traced to a psychogenic cause, and the condition cleared up under psychotherapy. JAHR, Omaha.

DERMOID CYST OF THE MIDBRAIN. E. H. BAXTER and G. B. HABER, J. Pediat. **4**:795 (June) 1934.

A case of dermoid cyst of the midbrain in a white boy, 12 years old, is reported. There were symptoms of tumor of the brain and of hypopituitarism (Fröhlich's syndrome). At autopsy it was found that the cyst had caused a marked increase in intracranial pressure and internal hydrocephalus and also had produced pressure atrophy of the pituitary gland. LEMASTER, Evanston, Ill.

ACUTE POLIOMYELITIS AS A PRIMARY DISEASE OF THE CENTRAL NERVOUS SYSTEM. HAROLD KNIEST FABER, Medicine **12**:83 (May) 1933.

Poliomyelitis is essentially an infectious disease of the central nervous system caused by a neurotrophic virus which spreads along the axis-cylinders; it is not the result of generalized infection with localization in the nervous system. The virus enters the body through the nasal mucosa and proceeds along the olfactory nerves to the olfactory bulb and thence to the hypothalamic area, thalamus and perhaps the olfactory cortex. The main pathway then leads from the thalamus downward through the spinothalamic tracts to the posterior horn cells and from there to the anterior horn cells, directly or by way of the dorsal root ganglions. While anatomic, pathologic, experimental and clinical findings seem to show that this is the main pathway, numerous other nerve pathways are possible.

The disease is divided into four phases. The first or initial stage consists of psychic disturbances and disturbances of sleep, of the vegetative nervous system, of the mechanism of vomiting and of general sense reception (pain and hyperesthesia), with headache and fever. These symptoms can be explained on the basis of invasion of the midbrain, especially the hypothalamus and thalamus. The second phase, which is due to invasion of the posterior horn cells and posterior root ganglions, is characterized, in addition to many of the symptoms of the first phase, by localized pains and tenderness, stiff neck and pain or flexion of the spine, as well as ataxia, tremor and local weakness without paralysis. The third phase—that of paralysis—is due to invasion of the anterior horn cells by the virus, which in all instances acts directly on the cells to produce the injury, rather than to pressure caused by edema and perivascular infiltration. In the fourth phase, that of recovery, the residual paralysis is proportional to the damage done to the anterior horn cells by the virus.

The quiescent period in the disease may be during the time of axonal propagation; the "halting" process which occurs in many cases may be at the synapses of the neurons, where the antibodies from the blood stream come into contact with the virus. It is therefore essential in the use of convalescent serum (which should be from persons proved to have a high neutralizing titer) to give large amounts intravenously. Intrathecal administration probably is useless, as the direction of flow of fluids in the nervous system is from the perineuronal and perivascular spaces toward and into the subdural space. The tendency of the virus to die out in centers where conditions are not optimal may explain the phenomenon of "halting" during the course of the disease, as well as the nonparalytic cases.

MCBRYDE, Durham, N. C.

CONGENITAL SYPHILIS IN LOW-GRADE MENTALLY DEFECTIVE CHILDREN. K. C. L. PADDLE, Brit. J. Child. Dis. **30**:249 (Oct.-Dec.) 1933.

Of four hundred and two mentally defective children, mostly of low grade intelligence, thirty-seven, i. e., a total incidence of 9.2 per cent, were considered to have congenital syphilis.

Of these, twenty-seven showed a positive Wassermann reaction of the blood serum, three showed a positive macro-Meinicke clarification reaction of the blood serum; one showed a positive Wassermann reaction of the cerebrospinal fluid only; four had abnormal cerebrospinal fluid (the diagnosis congenital syphilis was confirmed by physical examination or the family history), and two had congenital syphilis with serologically negative reactions.

LANGMANN, New York.

PSYCHONEUROSES OF CHILDREN. J. CATHALA and A. BOSQUET, Arch. de méd. d. enf. **37**:449 (Aug.) 1934.

The practical importance of psychoanalysis in the clinical examination of children is stressed by these French investigators. They point to the frequent difficulty of diagnosis and treatment in patients apparently suffering from organic diseases that are of a purely functional nature, and assert that, without prejudging the

manner in which defects in the moral and intellectual spheres are reflected in the physical health, problems in the latter cannot be satisfactorily solved until those of a psychoneurotic nature are solved.

Several cases of apparent organic disease cured by suggestion are reported.

AMESSE, Denver.

PROPHYLAXIS OF INFANTILE PARALYSIS. ROHMER, WILLEMIN-CLOG and WALLGREN, Bull. A. internat. de pédiat. prevent. **1**:12 (Sept.) 1933.

At the third general conference of this association, which was held at Luxemburg in September 1933, the problem of the prevention of poliomyelitis was accorded chief place on the agenda. Exhaustive contributions were made by the authors, and the discussion by participating members of the society following these presentations led to further plans for the control of this disease. The summary and conclusions follow:

Regarding positive data to be used for the planning of prophylaxis the nasopharyngeal mucus and the salivary glands furnish the virus with the means of both entry and elimination; the intestines seem to serve only exceptionally.

In all probability, transmission is by human contact—a thesis that is strongly supported by many clinical and epidemiological observations and is accepted by almost all writers on the subject. Transmission by water (Kling's theory) is possible, but is rarely effected. Infection by milk and contaminated objects has also been noted.

The duration of incubation seems to vary from ten to fourteen days; the period of contagion does not appear in general to extend beyond three weeks after the outbreak of the disease.

The virus of poliomyelitis spreads with extreme rapidity among the population of a contaminated district. The morbidity is low, however; the greater number of persons are immunized by occult immunization or were immunized during a previous epidemic. Ninety per cent of urban populations and 50 per cent of rural populations are found to be thus immunized. Eighty per cent of the cases observed in a region where the infection was endemic were those of children under 6 years of age, who had not had the chance to be immunized.

With regard to prophylaxis, diagnosis of the disease and the isolation of patients are indispensable in both the classic forms and the much more numerous abortive forms; to aid in this end the principal clinical signs of the abortive forms and of the paralytic phase of the disease are recalled.

Starting from the biologic and epidemiological data just outlined, the authors lay down the following rules for prophylaxis: (1) early detection of the disease and isolation and specific treatment of all patients, including those with abortive cases; (2) seroprophylactic treatment of the whole population—or of the children only—by means of specific serum drawn from convalescent patients, monkeys or horses, or of the ordinary serum of adult human blood. It is urgent that sufficient stocks of specific serums be created in readiness for use in epidemics; (3) the establishment during every epidemic of a central medical organization empowered to prescribe the measures to be applied and to collect observations for future scientific use; (4) measures for disinfection and for the supervision of foodstuffs by departments of health; (5) measures to prevent the spread of infection by forbidding gatherings that might bring together inhabitants of the contaminated region and persons of other districts, and (6) in all countries, compulsory reporting of both epidemic and sporadic cases.

AMESSE, Denver.

POSTENCEPHALITIC MYOCLONUS AND GIGANTISM IN A GIRL TWELVE YEARS OLD. J. HALLÉ and P. ARONDEL, Bull. Soc. de pédiat. de Paris **31**:129 (March 21) 1933.

A girl, 12 years old, was admitted to the hospital because of gigantism, which began to manifest itself two years previously, and myoclonic contractions of the face and the right upper extremity, which appeared about five months before

admission. She was well except for these two disorders, and no other physical abnormalities were found during her stay in the hospital. In her history it was discovered that she had been acutely ill for about ten days four years previously and was then thought to be suffering from grip; it is believed that she had encephalitis at that time and that the myoclonus and gigantism were late sequelae. Intravenous injections of sodium salicylate were followed by marked improvement in the myoclonic contractions, which gradually disappeared. She was observed for some time after she left the hospital, and no return of this symptom had occurred. Its reappearance is considered probable.

BENJAMIN, Montreal, Canada.

TWO CASES OF STAPHYLOCOCCIC MENINGITIS. L. BABONNEIX and RIOM, Bull. Soc. de pédiat. de Paris **31**:139 (March 21) 1933.

Two acutely ill girls, 11½ months and 2 years old, respectively, were admitted to the hospital. They soon showed signs of meningitis. In the first case the spinal fluid, blood and urine contained staphylococci. The child became rapidly worse and died a few days after admission. No necropsy was performed. In the second case there was a localized collection of staphylococcic pus in the dorsolumbar region, and at autopsy it was observed that the pus extended up into the spinal canal as far as the eighth dorsal vertebra. The twelfth dorsal and fourth lumbar vertebrae showed small foci of osteomyelitis. No pus was encountered within the cranial cavity. All the organs were normal.

BENJAMIN, Montreal, Canada.

LOCALIZED NEUROFIBROMATOSIS OF THE LEFT ARM, WITH RAPID DEVELOPMENT OF PARALYTIC MANIFESTATIONS IN A GIRL OF NINE YEARS. ROBERT FROYEZ, Bull. Soc. de pédiat. de Paris **31**:202 (April 25) 1933.

A girl, 9 years old, had a large number of neurofibromatoses on the left arm. The diagnosis was confirmed by biopsy. Soon afterward she began to show weakness of some muscle groups of the left upper extremity, and these became paralyzed within about three months. This was probably due to involvement of certain fibers of one of the trunks of the brachial plexus.

BENJAMIN, Montreal, Canada.

INFANTILE PARALYSIS. M. TAILLENS, Bull. Soc. de pédiat. de Paris **31**:204 (April 25) 1933.

This disease afflicts persons of the Anglo-Saxon and Teutonic races more than those of Latin origin. The importance of early diagnosis, so that the serum may be administered as early as possible in the course of the disease, is stressed. It is pointed out that many of the symptoms at the onset of the disease are those which may be found with any infection. Three signs are emphasized as diagnostic of the disease in its early stage: (1) absence of the knee jerks, (2) astasia-abasia and (3) abnormal spinal fluid findings, consisting of a slight increase in cells, which are chiefly polymorphonuclears, and a slight increase in the protein content. The sugar in the spinal fluid is normal, and the chlorides are diminished. No mention is made of rigidity of the spine and neck as characteristic signs which appear early in the disease. In the discussion it is pointed out that loss of the knee reflexes usually takes place just before the onset of paraplegia of the lower extremities, although in some cases paralysis may not ensue; in some cases the reflexes are exaggerated during the stage of meningeal irritation prior to their disappearance. Taking into account the factors which make the evaluation of the efficacy of serum therapy difficult, Taillens believes that it reduces the mortality, the incidence of severe cases and the percentage of marked paralysis when it is carried out in the early, so-called preparalytic, stage of the disease.

BENJAMIN, Montreal, Canada.

ARAN-DUCHENNE ATROPHY IN A GIRL OF TWELVE YEARS. L. BABONNEIX, M. LÉVY and J. DAVID, Bull. Soc. de pédiat. de Paris **31**:222 (May 16) 1933.

A girl, 12 years old, showed marked atrophy of the hands and the lower parts of the forearms. The condition was noticed about two years previously and was becoming progressively worse. No abnormalities were found on examination of the nervous system. The electrical tests showed some hypo-excitability to the galvanic and faradic currents, but no reaction of degeneration. No cervical ribs were present. The diagnoses considered were amyotrophic lateral sclerosis, syringomyelia and chronic anterior poliomyelitis due to hereditary syphilis. The child showed no signs of the latter disease, and no mention was made of any tests of the serum or spinal fluid; nevertheless, it was decided to institute antisyphilitic treatment.

BENJAMIN, Montreal, Canada.

INFANTILE PARALYSIS (POLIOMYELITIS) PRESENT FROM BIRTH. M. LANCE, Bull. Soc. de pédiat. de Paris **31**:229 (May 16) 1933.

A girl, 11½ years old, showed some paralysis of both upper extremities, and the case had been considered as one of birth palsy until Lance saw her. He noted that the paralysis of the upper extremities was not typical of that type of palsy, and when he examined the lower extremities he found that some of those muscles were paralyzed and atrophied. It was ascertained that the child had never raised her arms since birth. It is believed that the infection with the poliomyelitis virus may have taken place before birth.

BENJAMIN, Montreal, Canada.

TWO CASES OF CONVULSIONS FOLLOWED BY COMA, ASSOCIATED WITH SPASMOPHILIA AND APPEARING WITH THE ONSET OF INTERCURRENT DISEASE. M. COFFIN, Bull. Soc. de pédiat. de Paris **31**:345 (July 11) 1933.

Two children, 13 and 19 months old, had severe convulsions followed by periods of coma, during the course of whooping cough in the first case and of measles in the second. Both had tetany. With medication with sedatives and calcium they recovered. The spinal fluid was normal, and there were no motor disturbances. Such occurrences are common, whereas sequelae of meningo-encephalitis in the course of the contagious diseases are relatively rare. The prognosis is unfavorable in the latter, while it is good in the former.

BENJAMIN, Montreal, Canada.

ASTROCYTOMA OF THE FOURTH VENTRICLE WITH COMPLICATING ACUTE INFECTION. M. L. CHRISTOPHE, P. DIVRY and M. MOREAU, Rev. neurol. **2**:206 (July) 1933.

A case (with observations at autopsy) of an astrocytoma of the floor of the fourth ventricle is reported in a 6 year old boy, who had convulsions and fever following a mild infection. Several months later he had a generalized convulsion and difficulty in moving the left hand. Jacksonian convulsions began on the left side of the body. The head was held tilted to the left. A mild attack of grip caused profound drowsiness and seemed to aggravate the other symptoms—ataxia, headache and increased intracranial pressure. Tumor was diagnosed, and an operation was performed, but the child died. The authors consider the last phase due not to the tumor itself but to arachnoiditis ensuing from the acute infection, which blocked the fourth ventricle.

DAFFINEE, Boston.

PRODUCTION OF ABSCESS IN THE TREATMENT OF CHOREA. A. RESSMANN, Riv. di clin. pediat. **31**:1324 (Nov.) 1933.

Ressmann reports sixteen cases of children with chorea who were treated in the Ospitale Infantile Bambino Gesù in Rome. Various methods of treatment were tried. In six of the more severe cases treatment was by the hypodermic injection of from 1 to 1.5 cc. of oil of turpentine into the buttock; local inflam-

mation started, and a sterile abscess developed within about four days. The abscess usually opened and drained of itself; the body temperature rose to between 38 and 39 C. (100.4 and 102.2 F.). With the onset of the fever the activity of the patient became strikingly less; there was some return of the motor activity after the abscess began to drain, but the net result of the treatment was marked improvement. Ressmann recommends this method of treatment in severe cases of chorea.

HIGGINS, Boston.

INTRODUCTION TO THE PSYCHIATRY OF CHILDREN. JUAN PORTELL VILÁ, Arch. de med. inf. **2**:184 (April-June) 1933.

This is the third of a series of lectures on psychiatry of children. The author takes up the normal physiologic development of American, Cuban, Negro, Mulatto and German children. Psychometric tests, tables and explanations are included.

HERRON, Spokane, Wash.

POSTDIPHTHERITIC CHOREA. G. SCAFFO DE CASAS MELLO and AMILCAR J. CASAS MELLO, Arch. de pediat. d. Uruguay **4**:342 (Aug.) 1933.

This condition occurred in a child 6 years of age, following an attack of diphtheria and particularly the development of a serum reaction. The choreic symptoms became very severe and continued for two months. In the early stages there were meningeal symptoms. The limbs were in flaccid paralysis for a prolonged period, but recovery was complete.

SCHLUTZ, Chicago.

ASEPTIC BENIGN PURULENT MENINGITIS. FREDERICO EGGERS and LUIS PULIDO AROCA, Rev. chilena de pediat. **4**:380 (Aug.) 1933.

The authors report a case of this very rare condition in an infant. All the symptoms of a severe form of meningitis were present. Repeated spinal punctures showed turbid but absolutely sterile fluid. Complete recovery without any residual symptoms took place within about two weeks.

SCHLUTZ, Chicago.

ORGANIZATION OF CHILDREN'S COLLECTIVES AND THE ACTIVITY OF THE PHYSICIAN IN UTILIZING THEM AS PSYCHONEUROLOGIC DISPENSARIES. E. D. KAGANOVA, Okhr. Zdor. det. i Podr., nos. 5-6, 1933, p. 26.

In handling problem children an effort is made to make the members of the group under the supervision of a physician responsible individually and as a group. Thus through competition and comparison among different groups an attempt is made to draw them away from their bad habits, and to foster a sense of responsibility and a normal attitude toward their own actions and those of other persons. The family is invited to participate in the change, and by watching other children a mistake in handling their own may be demonstrated.

SEMENENKO-MCKHANN, Boston.

THE VEGETATIVE NERVOUS SYSTEM OF SUCKLINGS IN CEREBROSPINAL MENINGITIS. Z. S. SHUREKHOVA and E. P. OVTCHARENKO, Vrach. delo **17**:495, 1934.

On the basis of their studies of cases of epidemic cerebrospinal meningitis during the outbreak of 1931-1932 in Kharkov, the authors arrived at the following conclusions:

1. In all children but one (whose condition was grave and who died of the disease) there was a strong vagotonia, which was more pronounced the graver the general state was.

2. In cases with a mild evolution which ended in recovery there were weakly pronounced vagotonia and sympathicotonia.

3. One may assume that the disappearance of strong vagotonic symptoms and the appearance of sympathicotonic ones may serve as a favorable prognostic sign.

In most of the cases with troubles of nutrition and pneumonia in which the patients died there was vagotonia; the latter was not so pronounced as in menin-

gitis. In cases in which the condition was mild and ended in recovery sympathicotonia was noted. In two cases there was vagotonia when the state of the patients was grave, which changed to sympathicotonia when the condition improved. The authors state that normal and healthy children do not show any predominance of the tonus of the sympathetic or vagus system.

YAMPOLSKY, Atlanta, Ga.

NEUROLOGIC EXAMINATION OF INFANTS. ANNA G. SCHOO, Acta pædiat. **15**:181 (March 28) 1934.

This is a worth-while contribution to pediatric neurology which does not lend itself well to abstracting. It comprises a painstaking examination of the static and kinetic reflexes of Magnus and de Kleijn with reference to their occurrence and significance in infants. Numerous tables are included to illustrate the reflex behavior of infants at various age levels; the data for these were acquired by the author. The article contains a copious bibliography of the pertinent literature.

MCCUNE, New York.

A CASE OF ACUTE OTOGENOUS CEREBELLAR ENCEPHALITIS. AAGE WESTERGAARD, Hospitalstid. (supp.) **76**:107 (Nov. 16) 1933.

A boy of 12 years, who had been hospitalized late the previous year and who had symptoms of otogenous intracranial complication, was operated on. An unusually large perisinous abscess was found, which communicated with an extradural abscess in the posterior cranial fossa. This was drained, and the next day symptoms of cerebellar disease appeared on the same side. The diagnosis resolved itself into that of a left-sided cerebellar lesion with involvement of the eyelids on that side. There was distinct left-sided dysdiadokokinesia and pronounced ataxia on that side, with knee-heel and nose-finger signs. There was, further, at times conjugate deviation of the right eye and, finally, left lateral nystagmus, which was slowly synchronous with a pulsating sound in the ear, but without vertigo. The diagnosis was confirmed by means of the Romberg test, the walking test and the pointing test of Bárány. The pointing symptom appeared only on the first day when the patient was out of bed, but did not recur. The differential diagnosis is discussed, and the diagnosis made by exclusion is shown to be justified by the findings at operation.

VINTON, Brooklyn.

Diseases of the Eye

PROBLEM OF THE SQUINTING CHILD. LOUIS KAZDAN, Canad. M. A. J. **30**:406 (April) 1934.

The essential conditions always present in squint are (1) deviation of the visual axes of the eyes and (2) defect in fusion faculty. The other conditions are: (1) suppression of vision in the eye that is deviated; (2) amblyopia ex anopsia, or low visual acuity in the deviating eye, due to disuse or resulting from neglect or inefficient treatment; (3) a refractive error, and (4), in rare instances, congenital amblyopia.

Kazdan discusses the details of classification, etiology, diagnosis and treatment.

Emphasis is placed on two points: (1) early recognition and (2) early and efficient treatment by a medical eye specialist.

MOORE, Omaha.

ORBITAL PHLEGMON IN INFANTS AND OSTEOMYELITIS OF DENTAL ANLAGE. P. DEFOUG, Bull. Soc. d'opht. de Paris, March 1934, p. 180.

In two infants, aged 4 and 5 months, the beginning of the sickness was well recognized. There was a slight rise in temperature, together with a firm infiltration of the lid, which was pale. Above the alveolar processes of the incisor tooth were two small abscesses, in which staphylococci were found. The process progressed rapidly. It may have been due originally to endogenous infection. It

was believed that the infection in one case was due to perimamillary furunculosis in the mother. Two days after the onset the symptoms were generalized, and there was noticeable exophthalmos. This was relieved by puncture of the lower conjunctival sac. Free pus was found. Following drainage, a sequestrum was removed. The other patient had a similar onset, with protrusion of the eyeball, followed by thrombosis of the orbital vessels and death.

L. L. MAYER, Chicago. [ARCH. OPHTH.]

REMAINS OF EMBRYONIC IRITIS. BAUDOT and GAULT, Bull. Soc. d'opht. de Paris, March 1934, p. 183.

The authors report two cases of iritis of embryonic origin studied under the slit lamp. The first patient, a man of 47 years, showed along the temporal pupillary border an exudate made up of fine white vessels which moved with the pupil. Over this were fine brown-pigmented synechiae which ran from the border of the pupil to the anterior capsule of the lens. The left eye was similar. The patient had subacute glaucoma and a positive Wassermann reaction.

The second patient was a girl of 9 years. The lenses were congenitally subluxated below and outward. Secondary glaucoma had existed for more than two years. White synechiae of the iris, more marked during myosis, were noted at 6 o'clock. In neither case did the synechiae distort the pupils, a characteristic of the iritis occurring during embryonic life. Both patients showed signs of hereditary syphilis and secondary glaucoma.

L. L. MAYER, Chicago. [ARCH. OPHTH.]

BILATERAL CONGENITAL COLOBOMA OF THE UPPER LIDS. BONNET, PAUFIQUE and BONAMOUR, Bull. Soc. d'opht. de Paris, March 1934, p. 229.

Since the first description of this rare condition by Wilde, in 1862, reports of about one hundred and fifty cases have been published. The authors' case was complicated by a corneal dermoid and an acute ulceration of the center of the cornea. The dermoid was removed with a Graefe knife and studied histologically. Plastic repair was accomplished on both upper lids, with satisfactory results. The case was complicated by a nasal malformation, and this, together with the dermoid of the cornea, makes it of unusual interest.

L. L. MAYER, Chicago. [ARCH. OPHTH.]

SODIUM CHLORIDE CONTENT OF TEARS IN NORMAL AND DISEASED EYES. D. MICHAIL and P. VANCEA, Compt. rend. Soc. de biol. **115**:894, 1934.

The reported data on the sodium chloride content of tears show wide variations. In the latest results published (Roth, 1922), the average content found was 0.948 per cent.

With the use of blunt capillary pipets gently placed laterally in the lower culdesac, 0.1 cc. of tears can be collected in from three to ten minutes. In fifteen normal eyes the sodium chloride content, determined by the Volhard-Rousnjak technic, averaged 0.823 per cent. In acute ocular disease the salt content diminished on an average of 0.07 per cent, but in chronic cases the tears tended to become more salty, the average increase being 0.065 per cent.

J. E. LEBENSOHN, Chicago. [ARCH. OPHTH.]

CONGENITAL BILATERAL ECTOPIA OF THE LENS AND ARACHNODACTYLIA. KILLMANN, Klin. Monatsbl. f. Augenh. **92**:335 (March) 1934.

Congenital bilateral ectopia of the lens was found in 40 per cent of persons with arachnodactylia. Killmann reports eight cases of this type. One of them was atypical; it occurred in the 30 month old son of one of the patients. Two of the patients were females, and six were males. All were tall, their skulls were dolichocephalic, their features elongated; the chin was long in one of them, and their hands and feet were large. Curvature of the spine existed in four of them.

Contraction of the flexors of the fingers and toes, congenital disorder of the heart and flatfoot were further anomalies; the muscles and subcutaneous fat were underdeveloped.

Congenital bilateral ectopia of the lens was noted in the seven typical cases of arachnodactylia, concomitant strabismus in four and atrophy of the stroma and of the pigment layer of the iris in one. Changes in the fundus were present in three of these patients; glaucoma, in none.

Metabolic tests made in three patients did not reveal disease of the hypophysis; roentgenograms showed normal size and structure of the sella turcica and normal long bones, except in one boy aged 6, who had incomplete epiphyseal lines in the distal end of one metacarpus and the head of one metatarsus.

Dominant heredity was demonstrated positively in two and evidently in one patient by objective examination, and it was suspected from the history in two others. Syphilis, consanguinity and alcoholism could be excluded.

STOLL, Cincinnati. [ARCH. OPHTH.]

SIGNIFICANCE IN STRABISMUS OF SYMPTOMS OF DEGENERACY AND UNILATERAL PREDOMINANCE OF THE BODY. O. LIPPMANN, Klin. Monatsbl. f. Augenh. **92**:370 (March) 1934.

Lippmann discusses the theories of the etiology of strabismus and the question of the relation between the predominant hand and the predominant eye. He then reports his research on the relation between the prevalent use of one eye, one hand or one half of the body with the strabismic aberration of one eye. He found that strabismus is not a symptom of degeneracy. Stammering occurs as often with strabismus as without. Left-handedness does not favor the development of strabismus. The predominant side of the body influences the strabismic side, especially in patients who have isometropic and equal eyes. The left eye is generally more often strabismic than the right eye. Left-handedness in a person with an existing disposition to strabismus causes aberration of the right eye. The presence of a predominant eye does not cause disposition to the development of strabismus, if the eyes are otherwise equal.

STOLL, Cincinnati. [ARCH. OPHTH.]

Diseases of the Ear, Nose and Throat

COMPLICATIONS OF RETROPHARYNGEAL ABSCESS. LESTER ROSENBERG and MORRIS BERKE, J. Pediat. **4**:764 (June) 1934.

Retropharyngeal abscess is considered to be a very serious condition, requiring fine judgment for proper treatment. The frequent occurrence of sudden death from incision or spontaneous rupture of the abscess is mentioned. The frequency of severe hemorrhage, thrombosis or rupture through the external auditory canal is discussed. Several cases are reported. Fluctuation should preferably be presented before incision of the abscess.

LEMASTER, Evanston, Ill.

LUDWIG'S ANGINA, WITH REPORT OF CASES. DAVID ST. PIERRE ASBILL, South Carolina M. A. **30**: 55 (March) 1934.

Asbill reports six cases of Ludwig's angina in patients ranging in age from 5 to 65 years. He emphasizes two points: (1) carious and decayed teeth as important causative factors and (2) the necessity for early treatment by incision and drainage at the most pendant portion, preferably by the submental route.

WESTON JR., Columbia, S. C.

LYMPHADENOID TISSUE OF THE UPPER RESPIRATORY TRACT. HENRY VINCENT FORSTER, Lancet **2**:296 (Aug. 11) 1934.

"I find it difficult to agree with the recommendation that when a general anesthetic is given for removal of adenoids the palatine tonsils should also be sacrificed as a matter of routine."

It is not easy to decide how many attacks of tonsillitis a child may be allowed before becoming a subject for tonsillectomy, but it happens that children pass through such phases and then cease to be troubled by further attacks. Reddening of the faucial pillars does not necessarily signify chronic tonsillitis. Edematous infiltration of the tonsil, with associated redness and swelling of the palatal arches, is a definite indication of disease. Glandular enlargement in the tonsillar chain in the neck may be commonly felt; but the diagnosis of harmful enlargement may vary with the personal opinion of the observer, especially when the patient is a child. Conservative treatment is therefore advisable. But when it is noticed that frank glandular enlargement persists, tonsillectomy is indicated, no matter what may be the appearance of the tonsil itself.

The results of adenoidectomy in properly selected cases are often brilliant. It is time, however, to dispel the popular idea that when such an operation gives poor results the adenoid mass has returned and must be removed again. If the operation has been properly carried out, recurrence is rare. The development of residual granular nasopharyngitis should not call for the curet or the adenectome, but for an inquiry into the general condition of the child and particularly into the condition of the nose.

LANGMANN, New York.

SPONTANEOUS CURE OF A PULMONARY ABSCESS SECONDARY TO MASTOIDITIS WITH SINUS THROMBOPHLEBITIS. B. WEILL-HALLÉ, RICHIER and A. ABAZA, Bull. Soc. de pédiat. de Paris **31**:337 (July 11) 1933.

A girl, 8½ years old, had chronic suppurative otitis media for two years. Mastoiditis followed by thrombophlebitis of the lateral sinus and thrombosis of the right jugular vein developed. Two weeks after she had been successfully operated on she again showed hyperpyrexia, and it was found that she had a metastatic abscess of the apex of the left lung. During the following three weeks the abscess healed. There had been no vomiting and no special treatment.

BENJAMIN, Montreal, Canada.

PSEUDOMEMBRANOUS ANGINA DUE TO STREPTOCOCCIC INFECTIONS. LINO BUBANI, Pediatria **42**:295 (March 1) 1934.

Bubani reports two cases of pseudomembranous angina due to streptococcic infections, together with a detailed clinical analysis of the phenomena associated with such conditions. He points out that frequently it is possible to establish an approximately correct diagnosis from the clinical data alone.

SIGNORELLI, New Orleans.

INDICATIONS FOR TONSILLECTOMY. ALFREDO GRUNBERG SMITH, Rev. med. de los hosp. **2**:55 (Feb.) 1934.

To justify tonsillectomy there ought to exist chronic tonsillitis with either local or general symptoms or both. Smith describes these symptoms and the associated pathologic processes.

HERRON, Spokane, Wash.

DIAGNOSTIC SIGNIFICANCE OF MUCK'S EPINEPHRINE-SOUND EXPERIMENTS. ERNST E. GIERLICHS, Monatschr. f. Kinderh. **59**:321, 1934.

In 1922, Muck described a test on adults which Gierlichs attempted in children. The technic is as follows: A 1:1,000 solution of epinephrine is sprayed into the nose. This is repeated until the normal pale red mucosa becomes silver gray. Then the sound is introduced and is passed over the mucosa two to three times, an effort being made to keep it in the same track. In normal persons the site of the application of the sound reddens, an area of vasodilatation appearing in the center of the generalized vasoconstriction.

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Among seventy-five apparently normal school children the reaction was normal in all but nine. More detailed examination showed that of these nine four suffered from syphilis, three from migraine, one from umbilical colic and one from an undetermined condition. The reaction was not positive in children who suffered from spasmophilia in infancy. Gierlichs concludes that the test is of value in distinguishing the group of children with abnormal vasomotor reactions. An incidental conclusion is that certain forms of umbilical colic, when not due to appendicitis, belong to the vasomotor group.

GERSTLEY, Chicago.

Diseases of the Skin

CUTANEOUS MANIFESTATIONS OF ALLERGY. CHARLES MALLORY WILLIAMS, Arch. Dermat. & Syph. **29**: 333 (March) 1934.

This article is on immunity and its relation to allergy. Williams mentions especially secondary cutaneous lesions as they occur in syphilis, tuberculosis and tinea. He discusses various erythematous rashes seen in bacterial infections and urticaria and eczema as due to food allergy. Contact dermatitis as an allergic manifestation is also discussed.

DULIN, Iowa City.

URTICARIA: ETIOLOGIC OBSERVATIONS. J. G. HOPKINS and B. M. KESTEN, Arch. Dermat. & Syph. **29**: 358 (March) 1934.

In this article the many etiologic factors of urticaria are discussed. The antigen-antibody reaction of horse serum is described in detail, and comparison to this is made in the explanation of urticaria developing from food eaten a few days previously or from the overeating of foods which had heretofore caused no disturbance. Cases in which urticaria occurred from food, drugs, inhalants, focal infections, heat, cold and menstruation are cited, and the fact that in some cases the psychogenic factor plays an important rôle is pointed out. Cutaneous tests were found to be of little practical value in this form of allergy.

DULIN, Iowa City.

THE RELATION OF PAPULAR URTICARIA AND PRURIGO MITIS TO ALLERGY. ABRAHAM WALZER and MAX GROLNICK, J. Allergy **5**: 240 (March) 1934.

A detailed description of these two diseases is given, and a comprehensive report is made of the work done to show their relationship to allergy. The authors conclude: "1. Papular and prurigo mitis (Kaposi) are probably atopic illnesses. 2. Positive skin tests obtained in patients with papular urticaria and prurigo mitis bear no relation to other atopic conditions associated with them. Skin testing in papular urticaria and prurigo mitis is of no diagnostic or therapeutic value."

HOYER, Cincinnati.

ACTIVE TRANSMISSION OF URTICARIA BY BLOOD TRANSFUSION. MILO K. TEDSTROM, J. Allergy **5**:303 (March) 1934.

A man suffering from aplastic anemia showed generalized urticaria thirty minutes after receiving 500 cc. of whole blood intravenously by the direct method. He had no previous history of any allergic phenomena.

The donor had generalized hives at the time of the transfusion, resulting from the ingestion of strawberries, to which he was sensitive.

The urticaria in the recipient was relieved by epinephrine. Subsequent ingestion of strawberries did not produce urticaria. He received another transfusion two weeks later from the same donor without having hives; the donor at the time was free from hives.

Tedstrom expresses the belief that a "histamine-like" substance was transmitted in the blood in the first transfusion, and he stresses the importance of investigating the allergic history of prospective donors.

HOYER, Cincinnati.

THE TREATMENT OF HEMANGIOMATA BY EXCISION. JOHN STAIGE DAVIS and HERBERT E. WILGIS, South. M. J. **27**:283 (April) 1934.

Davis and Wilgis believe that the treatment of hemangiomas by excision is safer for the patient in the hands of a surgeon with a reasonable amount of skill and experience than is the treatment of these tumors by radium or the x-rays, unless the patient is in the hands of an expert. If the latter treatment is used, there is danger of burns and of atrophy and a check of development of bone and adjacent tissues following irradiation. The same possibilities exist with the injection method, and pulmonary emboli and extensive sloughs may follow the injection of sclerosing solutions.

SCHLUTZ, Chicago.

THE INFLUENCE OF ULTRAVIOLET RAYS ON ERYTHEMA NODOSUM. D. MÓRITZ, Arch. de méd. d. enf. **37**:476 (Aug.) 1934.

P. Woringer classified the cutaneous reactions seen in the course of various infectious diseases as immunizing and allergic; an example of the former is the response of the skin to vaccination against smallpox, while the latter is represented particularly by the reaction of infected subjects to tuberculin.

That certain factors influence the reactivity of the skin has long been recognized. For example, heat augments the intensity of vaccination, while cold inhibits it; viosterol, either applied locally or administered by the gastro-intestinal tract, diminishes the reaction to tuberculin. Among these agencies, both stimulating and restraining, the rôle of irradiation is the best known. Bentivoglio first demonstrated that the cutireaction to tuberculin is less intense on skin recently exposed to the ultraviolet rays than on areas not subjected to irradiation; Woringer observed the influence of ultraviolet rays on cutaneous reactions, both immunizing and allergic, and found that the former was accelerated and the latter impeded.

Erythema nodosum is a disease of the skin the etiology of which is still a matter of dispute. Although the majority of writers, particularly pediatricians, consider it a cutaneous manifestation of tuberculosis, there are some, notably dermatologists, who classify it as a specific infectious disease. To determine in which category—immunizing or allergic—erythema nodosum belongs, Móritz of Budapest carried out some experimental work on a suitable subject. The entire body, with the exception of one lower limb, was wrapped in black linen and exposed daily to the ultraviolet rays. It was found that the involution of the nodules was much more rapid on the area exposed than on the parts which were covered and, furthermore, that new crops of nodules were more rare and the eruption less intense on the parts irradiated. The action of ultraviolet light, then, is the same in this disease as in the tuberculin reaction, justifying the conclusion that there is evidently a marked resemblance in the mechanism of these phenomena. Móritz argues for the recognition of erythema nodosum as an allergic reaction to a tuberculous organism, which may be provoked by both specific and nonspecific factors.

AMESSE, Denver.

A LITTLE SIGN OF MOLLUSCUM CONTAGIOSUM. A. TZANCK and PAUTRAT, Bull. Soc. franç. de dermat. et syph. **41**:237 (Feb.) 1934.

Molluscum contagiosum seldom offers any difficulties as to diagnosis, but a diagnostic sign claimed to be thoroughly reliable is offered by Tzanck and Pautrat for the identification of doubtful cases. A fine jet of ethyl chloride is sprayed on the suspected lesion, and at the moment when whitening occurs a tiny crystalline circle, surrounding the lesion and sharply limited to it, stands out clearly. This phenomenon has been found to take place with remarkable constancy in cases of molluscum contagiosum and to be absent consistently in cases of other types of papules, such as warts and lesions of lichen planus or syphilis.

GANDY, Houston, Texas.

A Case of Pellagroid Caused by Injections of Trypaflavine. M. Murayama, J. Orient. Med. **20**:66 (May) 1934.

A 6 year old boy received twenty injections of acriflavine hydrochloride because of an inflammation of the right eye. After the last injection an erythematous itching eruption appeared on the neck and the dorsa of both hands. Bullae formed, and a mild desquamation followed. Murayama diagnosed the condition as pellagroid caused by injections of acriflavine hydrochloride. LeMaster, Evanston, Ill.

Surgery and Orthopedics

Surgery of Infancy and Childhood. Edward J. Donovan, New York State J. Med. **34**: 187 (March 1) 1934.

This brief review of surgery in infancy and childhood considers early diagnosis, the preoperative and postoperative administration of saline solution, transfusions, acidosis, status lymphaticus and anesthesia. Aikman, Rochester, N. Y.

Sympathectomy. E. D. Telford, Lancet **1**:444 (March 3) 1934.

In this article, which is a review of one hundred operations, the term sympathectomy is limited to the operation of cord ganglionectomy in the lumbar and cervicodorsal segments of the autonomic system.

Sympathectomy was performed in forty-five cases of thrombo-angiitis obliterans, twenty-two cases of Raynaud's disease and nine cases of acrocyanosis.

Three patients with anterior poliomyelitis of the lower extremities were subjected to lumbar sympathectomy in the hope of delivering an increased volume of blood to the limb. Up to the present the results have been satisfactory.

In Hirschsprung's disease a good result may be expected from sympathectomy only in cases in which there is still a sufficiently normal colonic wall capable of response to the altered innervation. Of the operations recommended, that which breaks the sympathetic and conserves the parasympathetic supply seems the more sound physiologically. An excellent result is reported in an 8 year old boy.

Other conditions in which sympathectomy was done include constipation, hyperhidrosis, scleroderma and sclerodactylia. Langmann, New York.

The Pathology of Acute Strangulation of the Intestine. Robert L. Holt, Brit. J. Surg. **21**:582 (April) 1934.

In this paper the results of the experimental work are clearly given in the author's conclusions, which are as follows:

1. The duration of survival following venous strangulation of the intestine varies directly with the length of bowel affected.

(*a*) When long loops are strangulated there is no evidence of any toxemic process, and death is due solely to the withholding of a large volume of blood from the circulation by the loop.

(*b*) When moderate-sized loops of intestine are strangulated insufficient blood is withheld from the circulation to bring about a fatal issue, and death results from the absorption, via the peritoneal cavity, of the fluid exuding from the loop, which becomes highly toxic about twenty hours after the onset of strangulation.

(*c*) When short loops are strangulated there is neither sufficient blood withheld from the circulation nor sufficient toxins absorbed to cause death. Perforation of the loop always precedes death, which follows from the resulting widespread peritonitis aided by the absorption of the toxic contents of the loop. Only rarely is the latter the sole agency in bringing about a fatal result.

2. The toxic qualities of the peritoneal exudate from a strangulated loop result from the action of proteolytic organisms on the tissues of the intestinal wall. The exudate is not derived from the contents of the lumen of the loop.

3. There is no support for the view that bacterial exotoxins (e. g., Bacillus Welchii) are responsible for the toxemia of acute strangulation. Evidence is

brought forward which suggests that the toxin is of large molecular form and probably akin to the proteoses.

4. It is suggested that when very small loops are strangulated in extraperitoneal positions, e. g., femoral hernia, the cause of death is the dehydration resulting from the obstruction of the small intestine which accompanies the strangulation.

5. When the arteries as well as the veins are obstructed in strangulation death follows from a combination of toxemia and peritonitis resulting from the action on and the penetration of the intestinal wall by bacteria from the lumen.

SUMMERFELDT, Toronto, Canada.

THE GREAT TROCHANTER IN INFANCY: ILIODIAPHYSEAL ARTHRODESIS BY THE EXTERNAL ROUTE IN COXALGIA IN YOUNG INFANTS. A. DELAHAYE and DUPUIS, Arch. franco-belges de chir. **33**:1033, 1932.

Up to 10 or 12 years of age the bony mass of the trochanter is buried in a cushion of cartilage varying in thickness from 2 to 5 mm. Its blood supply is poor and has no large anastomotic connections. In consequence of this deficiency operation on the great trochanter in infancy entails a risk of trophic disturbances of the bone. Furthermore, in iliotrochanteric arthrodesis at this age there is a poor soil for implantation. This lends force to a criticism made by the authors on a case in which an operation of this nature was performed, in which an intertrochanteric pseudo-arthrosis had formed, due probably to the change brought about in the vitality of the bony mass of the trochanter. To avoid this misfortune they advise external iliodiaphyseal arthrodesis. An osteoperiosteal S-shaped graft is taken from the tibia and used to join the wing of the ilium with the femur in its upper external portion where the tissue of the bone is not dense.

VINTON, Brooklyn.

SOME OPERATIONS FOR INFANTILE PARALYSIS OF THE LOWER LIMBS. E. SORRELL and L. MÉRIGOT, Paris méd. **1**:528 (June 16) 1934.

Sorrell and Mérigot favor a suspension method for this condition and discuss this treatment in relation to isolated paralysis of the extensors, the triceps group, the motor muscles, the quadriceps and all the groups of muscles.

SANFORD, Chicago.

ACCIDENTS IN EXTRAMUCOUS PYLOROTOMY FOR HYPERTROPHIC STENOSIS IN INFANTS. RAYMOND LEIBOVICI, Presse méd. **42**:535 (April 4) 1934.

Commenting on the usual happy results of pylorotomy for pyloric stenosis, the author reports two cases which presented particular problems and which are rarely noted. Following operation the first patient continued to vomit, despite an apparently successful operation. An idiosyncrasy was suspected, and the baby was found to be sensitive to cow's milk. An adjustment of his diet resulted in the cessation of vomiting. Vomiting following operation may lead one to suspect incomplete resection of the tumor, hyperexcitability of the stomach or digestive intolerance. The ratio of cell chloride to plasma chloride is of great value in determining whether the operation was complete or not, as the ratio returns rapidly to normal if the pyloric section was successful.

The second case was one in which the duodenal mucosa was nicked during the course of the operation. Recovery was uneventful. The extreme fragility of the tissues in the infant render this accident extremely likely, but it is easily repaired. Postoperative care assumes even more importance in cases in which accidents occur. Particular care must be taken that all the fibers surrounding the duodenopyloric junction are severed.

BIEKER, St. Petersburg, Fla.

Miscellaneous

THE CHILD'S PHYSICIAN. REGINALD H. WIGGINS, Arch. Pediat. **51**:141 (March) 1934.

Wiggins stresses the responsibility of the physicians entrusted to give advice on the training and care of children. He believes that the pediatrician steps to the forefront of physicians, as the task of advising on the training and care of future citizens is tremendously worth while. He further points out the training necessary for one in a position to give advice to parents on how to rear and train children.

WADDELL JR., University, Va.

CHILD HEALTH 1933-1934. MARTHA M. ELIOT, J. Pediat. **4**:817 (June) 1934.

Eliot states that the purpose of this review is to set forth certain pertinent facts regarding the depression and its effect on child health and child health services, to point out some of the steps that have been taken to stimulate interest in these problems and to attempt to safeguard the health of children in the future. Even in normal times the need for more adequate child health work was great; the depression has increased it many times. The salient features of the reports on child health during the past few years are discussed. Other topics considered in this review are the appropriations for child health in 1933 and 1934, child health activities, the Pennsylvania emergency child health activities and the child health recovery program. There now seems to be little doubt that the depression has been having an adverse effect on the health and nutrition of many children. With the present limited health budgets and the relatively low standards of relief still prevalent in many communities, joint action on the part of health and medical groups is imperative.

LEMASTER, Evanston, Ill.

THE ACTION OF ULTRA-VIOLET RAYS. LEONARD HILL, Brit. J. Phys. Med. **9**:7 (May) 1934.

Sir Leonard Hill describes the biologic action of the ultraviolet ray and discusses its uses and limitations.

HARTMAN, Cleveland.

LEAD POISONING IN CHILDREN. T. STANLEY RODGERS, Lancet **1**:129 (July 21) 1934.

Apart from industry, lead poisoning occurs more commonly in children than in adults, for three reasons: 1. The young child frequently conveys to his mouth anything that he can get hold of. Pica is not uncommon. 2. Children are liable to suffer from acidosis, and this may precipitate toxic manifestations in a case of latent poisoning. 3. The young are very susceptible to lead.

The action of the poison and the symptomatology of lead poisoning are discussed. Lead encephalopathy is the most serious of the acute manifestations and is common. The prognosis in encephalopathy is serious.

Similar but not identical roentgenographic appearances are seen in scurvy, congenital syphilis, Albers-Schönberg disease and poisoning by vitamin D, elementary phosphorus and other heavy metals, such as strontium and bismuth.

The possibility of lead poisoning should be considered in cases of convulsions of obscure origin, papilledema and ocular palsy without obvious cause and in cases of anemia with colic or peripheral palsy of the limbs.

The treatment is discussed, and a case in a 2 year old boy cited.

LANGMANN, New York.

BASIS AND AIMS OF CHILD PROTECTION DURING THE PRESCHOOL AGE. ERNESTO NELSON, Bol. Inst. internac. am. de protec. a la infancia **7**:393 (April) 1934.

This article deals with the condition of the child of preschool age in Argentina; the statement is made that in that country there are about one million children from 2 to 6 years of age.

Recent statistics on physical defects among children entering school reveal the fact that even among the well-to-do classes young children are not taken care of in a measure consistent with their needs. Nelson also shows that during the period of growth physical defects increase with age. It is obvious, then, that preventive measures should be begun as soon as possible.

Such measures should be a continuation through the preschool age of most of the services for infants, and, on the other hand, young children should benefit from proper anticipation of some of the educational and hygienic services for the children of school age.

In regard especially to the latter line of protection, Nelson found that the chief agencies that in several countries have attended to the needs of young children from a hygienic, educational and social angle are the crèche, the day nursery, the *casa dei bambini*, the *école maternelle* and the kindergarten.

Analyzing the needs that these institutions strive to fill, as well as the ways in which service is rendered, Nelson sees the need of integrating their hygienic, educational and social activities into a coordinate whole in one single institution which might well be the so-called nursery school, which is rapidly spreading throughout Europe and the United States.

In view of the fact that the public is not entirely familiar with the nursery school, Nelson describes at length the typical activities of its most perfect models and shows that such an institution offers excellent opportunities for centralization of the most important services that preschool children are in need of.

He summarizes in the following items the chief features of a well administered nursery school: (*a*) sharing of the child in the making of his own life, (*b*) participation of the child in the life of the community, (*c*) contact with nature, (*d*) awakening the child's interest in home-making, (*e*) giving the child opportunities for play, (*f*) giving assistance in problems of nutrition, (*g*) providing for social development, (*h*) development of the child's personality, (*i*) keeping the child at par with his native possibilities, (*j*) preventing and eliminating behavior maladjustments, (*k*) transferring to the home the newly acquired habits and reactions, (*l*) educating the parents and (*m*) insuring freedom for the parents, without depriving them of contact with the child's daily activities.

AUTHOR'S SUMMARY.

BIOLOGY OF THE SCHOOL CHILD. HANS HUMMEL, Arch. f. Kinderh. **101**:147 (Feb. 28) 1934.

In 1932 and 1933 measurements were made of the weight, height, circumference of the chest and expansion of the chest of the school children of Jena. These measurements are compared with those of the school children of the same locality made in 1921 and 1880. The significance of the findings is discussed.

LEMASTER, Evanston, Ill.

UNEXPECTED AND SUDDEN DEATH IN CHILDHOOD. S. A. SIWE, Upsala läkaref. förh. **39**:203, 1934.

This article is based on the study of two hundred and twelve cases of unexpected or sudden death in the first fifteen years of life. Most of the cases occurred in the first months, and in the majority death was due to diseases of the respiratory organs. Such diseases may not give rise to local symptoms and are easily overlooked. Even at necropsy the extent of the infectious lesion may be limited. In nurslings simple coryza or a slight intestinal disturbance may lead to vomiting and aspiration which rapidly and sometimes unnoticed end in death. In none of the cases studied did enlargement of the thymus appear to play any rôle in causing death. The possibility of respiratory aspiration does not seem to be recognized sufficiently. At necropsy it is not enough to inspect the finer bronchi for gastric contents. Litmus paper must be used in order to be sure that aspiration of gastric contents is not overlooked.

[ARCH. PATH.]

HEIGHT AND WEIGHT IN CHILDREN. MONRAD, Ugesk. f. læger **96**:215 (Feb. 22) 1934.

Previous statistical tables were found to differ in regard to the values for height and weight of children obtained in recent years. The average height at birth has increased from 50 to 51 cm., and the weight from 3,300 to 3,500 Gm. Monrad gives the following table:

Weight and Body Proportions During the First Year

Age	Height, Cm.	Weight, Gm.	Circumference, Cm.	
			Head	Chest
At birth	51	3,500	34	32
At end of				
1 month	55	4,000		
2 months	59	4,800		
3 months	62	5,500	41	37
4 months	64	6,100		
5 months	66	6,700		
6 months	67	7,200	43	41
7 months	68	7,600		
8 months	69	8,000		
9 months	70	8,400	45	43
10 months	71	8,700		
11 months	72	9,000		
12 months	73	9,300	46	45

ELGHAMMER, Chicago.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

Jan. 10, 1935

HARRY T. BAKWIN, M.D., *Chairman*

ALEXANDER T. MARTIN, M.D., *Secretary*

LOCAL HYPERTROPHY AND ATROPHY OF FAT FOLLOWING INJECTIONS OF INSULIN IN CASES OF JUVENILE DIABETES. DR. ALFRED E. FISCHER.

The injection of insulin causes atrophy in the subcutaneous tissues of some children and hypertrophy in those of others. In a third group of children both atrophy and hypertrophy are present.

Roentgenographic and pathologic studies of the altered tissues in patients with this condition were made. White streaks, apparently strands of fibrous tissue, were visualized on the roentgenogram. On section the atrophied areas contained a decreased amount of adipose tissue, and there were infiltration by round cells and fibrosis. On the other hand, in the swollen or hypertrophied tissue the fat cells were large. There appeared to be an increase in the total amount of fat, and some edema and inflammatory changes were present.

The explanation for the hypertrophy of the subcutaneous tissue is at present obscure. It may represent an actual local deposit of fat as the result of some unexplained action of the insulin. On the other hand, the tissue changes may result from an inflammatory reaction produced in the subcutaneous tissues by the injection of solutions of insulin.

Roentgenograms and sections of the atrophied and hypertrophied tissues were demonstrated.

VITAMIN B SUPPLEMENTS DURING INFANCY. DR. HERBERT L. ELIAS AND DR. REUBEN TURNER.

During the past twenty-five years numerous experiments on animals and clinical studies have shown that vitamins B and G are essential for growth and lactation. Following the reports that these two vitamins are growth-stimulating and following the observations of Mendel in 1917 and of Macy in 1927 that milk is not a good source of at least vitamin B, many clinical investigators attempted to accelerate the growth of infants by enriching their diets with extra amounts of both vitamin B and vitamin G.

In December 1932, with the aid of a grant from Mead Johnson and Company, an extensive clinical investigation of vitamins B and G was started on the obstetric service and the children's medical service of Bellevue Hospital. The purpose of this investigation was threefold: (1) to determine the effect of vitamin B and G supplements on the growth and development of artificially fed infants, (2) to determine whether lactation could be influenced by enriching the vitamin B and G content of the maternal diet and (3) to study the effect of enriching the diet of pregnant women with vitamins B and G, noting especially the incidence of certain symptoms during pregnancy, labor and puerperium and the general condition of the new-born.

In the clinic for well babies we have observed a group of 238 artificially fed white infants for an average period of forty-six weeks. All of the infants were

seen for at least fifteen weeks and some for as long as two years. All infants who had any severe major illness requiring hospitalization were excluded from the study. There were no twins or premature infants included in this study and no infants suffering from any of the congenital or chronic diseases of infancy. A worker visited the mothers of these infants on the obstetric wards and instructed them to bring their babies to the clinic for well babies for the supervision of feeding and hygiene. All these babies were seen in the clinic only by the authors. None of the babies reported on in this group of artificially fed infants were born of mothers who received yeast in the clinic for prenatal care. The average age of the infants on entering the clinic was 3½ weeks. Infants not attending the clinic at least once every five weeks were excluded. The majority attended about every three weeks or more frequently.

All these infants received formulas of milk (1.7 ounces per pound, or 48.2 cc. per 453.6 Gm.) and water with about 1 ounce of added carbohydrate, the control group of 117 receiving plain dextrimaltose and the experimental group of 121 infants receiving dextrimaltose with added wheat germ and yeast, each ounce of this furnishing 300 Sherman units of vitamin B and 180 Sherman units of vitamin G. This preparation is marketed as Dextri-Maltose with vitamin B. All the infants received orange juice and 3 teaspoonfuls of cod liver oil from October to May. Cooked cereal was added to the diet during the fourth month of life, the group who were fed the vitamins getting Mead's Cereal, which contains added wheat germ and yeast, and the control group receiving a special cereal prepared exactly like Mead's Cereal but containing no wheat germ or yeast. Vegetables were added during the sixth month and egg yolk and scraped beef during the eighth and ninth months.

A chart shows the curves for weight of these two groups to be identical. The curves for the total body length and the curves for sitting height are also identical.

A second chart shows the percentage of infants suffering from one or more respiratory infections per age group. There is no constant difference in the incidence of these infections in these two groups.

The incidence of diarrhea is recorded in tables. The figures show no difference between the two groups in regard to attacks of diarrhea alone. These attacks are classified as to whether they occurred with or without a parenteral infection.

The next table shows that the infants fed the vitamins had anorexia less frequently than the control group. The beneficial effect of vitamin B in improving the appetite of vitamin-deficient animals has been frequently reported. However, in view of our inability to find other significant differences in this study we hesitate to draw any conclusions from these figures for anorexia.

In the prenatal investigation one group of 58 pregnant women received tablets of concentrated brewers' yeast, while another group of 60 attending the clinic at the same time served as controls. These two groups were treated exactly the same, except that the group given the vitamins was asked to eat eight tablets of concentrated brewers' yeast three times a day.

The first table shows that the age, parity, number of visits per mother, length of observation and weight of new-born were about the same in the two groups. The second table shows no difference in the incidence of certain symptoms of pregnancy in these groups. There were no cases of neuritis, toxemia or nephritis in either group. The next table shows no appreciable differences in some of the complications of labor. The incidence of prematurity and the neonatal mortality were not significantly different, there being two premature infants in the control group and one in the group in which the mothers received the vitamins; there were no deaths in the control group and one macerated infant born by breech delivery in the experimental group.

In the study of the effect of these vitamins on lactation a plan similar to the prepartum administration of brewers' yeast was followed. In 17 nursing mothers

taking twenty-four tablets a day the average length of lactation was 20 weeks, which is about the same as the 19.6 weeks of the control group. We do not believe that 17 cases are enough to permit the drawing of any definite conclusions.

In summary and conclusion, enriching the diet of pregnant women with extra vitamins B and G does not influence: (1) the incidence of certain symptoms during gestation, such as headache and dizziness; (2) the amount of loss of blood; (3) the severity of lacerations, and (4) the size and condition of the new-born.

Supplementing the diets of artificially fed infants with additional amounts of vitamins B and G does not exert a favorable influence on the rate of growth, the incidence of infections of the upper respiratory tract or the incidence of gastro-intestinal upsets during the period of life studied.

DISCUSSION

DR. BENJAMIN KRAMER: It is at times embarrassing to have to present what might be considered a "negative" paper, but no such feeling need attend the presentation of this contribution on the influence of vitamin B supplement during infancy.

There are undoubtedly virtues possessed by well balanced diets which cannot be improved on by vitamin supplements. In a carefully controlled investigation carried out under our direction by Dr. Gittleman and Dr. Weiner at the Brooklyn Hebrew Orphan Asylum, it was shown that the addition of extra vitamin C in the form of orange juice, vitamin D in the form of viosterol, and vitamins A and D in the form of haliver oil had no effect on the curve of weight, the curve of growth or the incidence of respiratory infections in the children fed the enriched diet, as compared with those fed the basal diet.

Those of us who are constantly urged for one reason or another to prescribe vitamin preparations can point to such well controlled observations as those reported by Dr. Elias and Dr. Turner as an argument against the use of vitamin B supplement when the basal diet is well balanced.

When diets are definitely deficient in vitamins it may become necessary to add such vitamin preparations. However, in the majority of instances it will probably be found cheaper to balance the diet than to add expensive vitamin concentrates.

RÔLE OF CHRONIC VITAMIN C DEFICIENCY IN THE PATHOGENESIS OF EXPERIMENTAL TUBERCULOSIS IN THE GUINEA-PIG. MERIDIAN GREENE, SC.D.; DR. MORRIS STEINER AND DR. BENJAMIN KRAMER.

This work, which was carried out in the pediatric research laboratory of the Jewish Hospital of Brooklyn, and which was made possible by a grant from Mead Johnson and Company, was undertaken with the object of determining the effect of chronic vitamin C deficiency on experimental tuberculosis in the guinea-pig.

Animals with chronic scurvy which were inoculated intraperitoneally with a large dose of a virulent human strain of tubercle bacillus, H37, showed no difference in survival, loss of weight or extent of tuberculous involvement as compared with control animals. When they were inoculated subcutaneously significant differences in survival and weight means were found as compared with the controls. The amount of tuberculosis was the same in the group with chronic scurvy as in the controls, but the latter died at a significantly later date. Chronic scurvy did not cause the development of generalized tuberculosis in animals inoculated with the relatively avirulent strain, R1. There was a significant difference in body weight between the animals with chronic scurvy and the controls at the termination of the experiment.

Acute scurvy produced no difference in the extent and severity of tuberculosis.

Guinea-pigs placed on a diet causing chronic scurvy and fed pure culture of H37 showed more extensive generalized and intestinal tuberculosis than did animals on a complete diet, even though the controls lived for a significantly longer period. When sputum was fed the findings were, in general, similar. However, macroscopic ulcers in the intestine were present in the majority of the animals with

chronic scurvy. In animals sensitized with the R1 strain and then fed the H37 strain extensive generalized or intestinal tuberculosis did not develop.

RELATIONSHIP OF THE MORPHOLOGY OF THE DIPHTHERIA BACILLUS TO ITS VIRULENCE. DR. LAWRENCE W. SMITH.

Routine analysis of 592 cultures from the nose and throat for virulent diphtheria suggested the modification of Wesbrook's classification into three major groups: the BL (blue type), the MG (metachromatic granular type) and the BT (bulging type—either with or without metachromatic granules). The latter group (236 cases) was uniformly 100 per cent virulent, while the BL type (250 cases) was only 38 per cent virulent, and the MG type (106 cases) was 61 per cent virulent. Of 396 virulent strains, 59 per cent were of the BT type. It is suggested from these results that tests for virulence carried out on animals might be dispensed with in cultures showing the BT type.

This in conjunction with the suggested modifications of technic in the performance of the test on animals would make for a significant saving in time and hospitalization of all avirulent carriers.

ELECTROCARDIOGRAPHIC CHANGES AND PERIPHERAL NERVE PALSIES IN TOXIC DIPHTHERIA. DR. EDWARD A. BURKHARDT; DR. CARY EGGLESTON, AND DR. LAWRENCE W. SMITH.

Serial electrocardiograms were taken in a group of patients with toxic diphtheria at Willard Parker Hospital. One hundred and thirty-four cases were included in the study, and electrocardiograms were taken every other day during the patients' stay in the hospital.

The electrocardiographic changes are easily placed in one of two groups: changes in the T wave and changes in the conduction system.

The first change noted was a slight decline in the ST line and a decreased amplitude of the T wave. The T wave then progressed to an iso-electric line and later to a negative T wave. It then slowly returned to normal in the reverse order of events. The average change began on the fifteenth day of the illness and lasted for twenty-five days. A table illustrating the changes and a slide of an electrocardiogram were shown. Twenty-three patients showed this change.

Eighteen patients showed changes in the conduction system, as manifested by splintering and prolongation of the QRS phase, arborization block, bundle branch block, auriculoventricular dissociation and ventricular escape. Thirteen of this group died. The first change began on the fifth day and the latest on the thirteenth day. The average duration was five and one-tenth days. (A table illustrating the group of changes and a slide of an electrocardiogram were shown.)

Many of the patients with electrocardiographic changes also had peripheral nerve palsies, as manifested by nasal regurgitation, nasal voice and other signs. (A table illustrating the onset and duration of the palsies was shown.)

Dextrose, atropine sulphate and barium chloride were used in an attempt to alter the graphic change and course of the disease. This experimental therapy resulted in failure.

The changes in the heart sounds and the clinical course of the disease were discussed.

Autopsy was performed in numerous cases, and special stains were used to determine the myocardial changes. Marked acute myocarditis was demonstrable. Myocardial fibrosis was shown in a young patient who died on the sixty-first day of the illness. (Photomicrographs in natural color were shown.)

BASAL METABOLISM OF TUBERCULOUS CHILDREN. DR. ANNE TOPPER AND DR. HAROLD ROSENBERG.

Tuberculosis is a chronic infection in which there are long periods of apyrexia associated with an active disease process. It therefore lends itself to a study of

the basal metabolic changes due to the infection per se, dissociated from any effect of fever.

Such a study is in progress on the pediatric service of the Sea View Hospital. The cases studied to date have been grouped as follows:

I. Extrapulmonary Tuberculosis (22 cases)

II. Pulmonary Tuberculosis

(1) Primary Infection (childhood type)

(a) Active (90 cases)

(b) Inactive (33 cases)

(2) Superinfection (adult type) (73 cases), including cases of Pneumothorax

(3) Pleurisy with Effusion (23 cases).

The preliminary results of this study were presented.

Feb. 14, 1935

HARRY BAKWIN, M.D., *Chairman*

ALEXANDER T. MARTIN, M.D., *Secretary*

APPENDICULAR TYPE OF BACILLARY DYSENTERY. DR. JOSEPH FELSEN and A. G. OSOFSKY, M.A.

The pseudo-appendicular type of bacillary dysentery (Sonne-Duval, Flexner) may be divided into typical and atypical types (asymtomatic, afebrile, constipation, appendicular and meningitic). These clinical types are based on studies of an outbreak of the Sonne-Duval type of dysentery in New York and the Flexner type of dysentery in Jersey City, N. J. The appendicular type constituted approximately 3 per cent of all the cases and was usually accompanied by mesenteric adenitis and acute distal ileitis (operative findings). These patients show a normal or subnormal leukocyte count, only a slight pyrexia, diarrhea, colic, abdominal tenderness (most manifest in the right lower quadrant), spasm of the ileum and sigmoid flexure (a mass may be felt in the right lower quadrant) and sigmoidoscopic evidence of acute colitis. The diagnosis is confirmed by cultural, phage and agglutination studies. Treatment is medical.

DISCUSSION

DR. S. KARELITZ: In the past five or six years I have had experience with a condition for which Dr. Felsen's work may offer an explanation.

From about September 15 to November 1 of each year I have seen in my practice several cases of bloody diarrhea coming on in children and within a few days affecting other members of the household. The disease has varied in severity from a very mild condition with no fever or only low grade fever, abdominal discomfort and occasional vomiting to a condition similar to typhoid fever, or true bacillary dysentery. In most cases the condition was self-limited, lasting only two or three days, but, less commonly, was of from twelve to fifteen days' duration in some instances. There were no eruption of the skin and no splenic enlargement, but in a few cases leukopenia as low as 2,000 white blood cells per cubic millimeter, with relative lymphocytosis, was found. Cultures of the stool usually yielded atypical Bacillus coli.

In the fall of 1933 and again in 1934 there were small epidemics of this condition on the pediatric wards of Mount Sinai Hospital. In 1933 it started with a diabetic child who had been on the ward for several weeks for regulation of diet. Suddenly fever of 101 F. developed, and he had several bloody soft stools. The condition lasted three or four days, after which he recovered, but almost every two or three days thereafter new cases of the same or an allied condition appeared. There were twelve in all. Some patients had abdominal pain, vomiting and fever, while most of them had bloody stools with abdominal pain and fever. Cultures of the stool showed the Flexner dysentery bacillus in one instance, the paratyphoid bacillus in another, and in the rest Bacillus enteriditis (Gärtner) and, most often, atypical B. coli.

Within from ten days to a month most children had in their blood corresponding agglutinins to the organism isolated from the stools.

Our experience in 1934 was almost identical with that of 1933. Dr. Louise Rauh, Dr. Jacob Brem and I attempted to trace the source of the infection in the food, but were unsuccessful. We assumed, therefore, that it must have spread from one child ill with this infection. Dr. G. Schwartzman, our bacteriologist, offered the suggestion that the condition in these cases might be of an unusual group of dysentery or paratyphoid fever, in which the cultural character or identification was either difficult or perhaps impossible to determine with available knowledge on the subject.

Perhaps our cases were similar to those of Dr. Felsen. In any event, they were not just cases of "intestinal grip." Patients with this condition should immediately be isolated so that contact infections may be avoided.

EVENTRATION OF THE DIAPHRAGM. DR. JOHN F. LANDON.

Eventration of the diaphragm is a rare anomaly best defined as an elevation of this structure permitting some of the abdominal contents to occupy the space normally containing the thoracic organs. The term eventration is misleading, as it implies an escape of viscera from the abdominal cavity, thus suggesting an opening in the diaphragm. In the great majority of cases this condition is congenital in origin and due to a failure of the primitive, peripherally situated premuscle masses to continue their normal centripetal growth, resulting in a diaphragm in which only a tenuous membrane remains in the mesial portion of the two diaphragmatic leaves.

The most common symptoms are cyanosis, dyspnea and dysphagia; the physical signs are inconstant. Diagnosis is very difficult, being commonly made by roentgenographic and fluoroscopic examinations. The differentiation of eventration from diaphragmatic hernia is of more than academic interest, as some cases of diaphragmatic hernia may be amenable to surgical intervention, whereas in eventration operation is commonly considered to be contraindicated.

Eventration is rare; less than one hundred cases have been reported. Its occurrence on the right side is especially unusual, justifying the presentation of a case of an infant observed from birth who died on the eighteenth day of life. Autopsy revealed the presence of the right lobe of the liver, the ascending colon, cecum, appendix and terminal part of the ileum in a sac consisting of thinned out diaphragm, which extended to the third rib anteriorly on the right side. The central portion of the right leaf of the diaphragm consisted of a thin, translucent membrane; the same condition existed on the left side but to a lesser degree.

Other congenital anomalies were absence of the middle lobe of the right lung, congenital heart disease with a defect of the interventricular septum and a bicuspid pulmonary valve.

DISCUSSION

DR. HARRIET C. MCINTOSH: The diagnosis of abnormality of the diaphragm in the new-born by roentgenograms is easy. Differentiation of the type of abnormality is more difficult, particularly when the lesion is on the right side. Eventration, as Dr. Landon has described, shows an elevated but intact diaphragm, with

the liver and intestine below it on the right and the stomach and intestine below it on the left, even though they may be located at abnormal thoracic levels. The differential possibilities from a roentgenologic point of view are: (1) absence of one half of the diaphragm, (2) hernias of various sorts and (3) paralysis of the diaphragm.

Absence of one half of the diaphragm and hernia through a very large aperture, rent or missing segment are indistinguishable roentgenologically. If the abnormality is on the left side, the striking picture resulting from filling of the left side of the chest by the stomach or intestine or both is unforgettable. It can always be demonstrated by barium sulphate in the intestine, and frequently without; the fluted honeycomb shadows bear little resemblance to any other condition except possibly multiple abscesses of the lung, which can be ruled out clinically as well as by a few swallows of barium sulphate. Of course there is no diaphragmatic outline, and no diaphragmatic movement can be seen under the fluoroscope, so no confusion with eventration can arise on the left. On the right, the diaphragm and superior surface of the liver conform to one another so that it is usually impossible for the eye to separate them, and differentiation is more difficult.

Smaller hernias on the left often show under the fluoroscope an intact diaphragm at a normal level and moving normally with respiration everywhere except at the herniated area. In hiatus hernia, the abdominal segment of the esophagus and the cardiac end of the stomach, and sometimes all of the stomach, slip upward through a relaxed esophageal hiatus. The condition is common in the aged; one observer reported its presence in 73 per cent of all old persons examined by means of the barium sulphate meal, but it is rare and merits little consideration in the new-born. Thoracic stomach is basically a short esophagus, with a stomach that has never descended, in part or at all, into the abdomen. It can be readily ruled out by barium sulphate, when part or all of the stomach is seen in the chest, with a bilaterally normal diaphragm below it.

Paralysis of the diaphragm in the new-born is due to injury of the phrenic nerve by obstetric maneuvers. It is usually accompanied by brachial paralysis. It shows an appearance on the x-ray film similar to that in cases of eventration, consisting of a high relaxed diaphragm on the affected side, sometimes with pressure atelectasis of the adjacent lung. Under the fluoroscope there is almost sure to be paradoxical movement in paralysis, a finding much more uncertain in eventration and not seen in the present case. I suppose that this is because the paralysis comes on suddenly, while the conditions entering into eventration have been developing slowly and the organs have become more or less fixed in place. There is an accompanying and interesting sign in paralysis, not so far reported specifically for eventration and not present in this case—a to-and-fro, seesaw movement of the mediastinal contents, produced by the same alternations of pressure that produce the paradoxical movement of the diaphragm itself. The syndrome of paralysis, unlike the signs described, can be recognized with equal ease on either side.

CHICAGO PEDIATRIC SOCIETY

Clinical Meeting, March 19, 1935

JOSEPH BRENNEMANN, M.D., *Presiding*

LIPODYSTROPHY; HEMIATROPHY OF THE FACE. DR. BERT I. BEVERLY.

CASE 1.—This 13 year old white girl was brought to the dispensary of the Children's Memorial Hospital three years ago because of a decrease in size of the right side of the face. From all the photographs and from the history it was evident that her face was symmetrical until six months previously. At the time of the examination there was a striking difference in the two sides. There was a

triangular depression of the right cheek which was due largely, if not entirely, to the disappearance of fat. There was no evidence of muscular weakness. Roentgenograms and measurements carefully taken at the University of Illinois School of Dentistry have shown no evidence of bony change. At times there have been neuralgiform pain and hyperesthesia of the same side. The results of neurologic examination were and have remained negative, except for a slightly suggestive Babinski sign on the left side. Six months following the patient's first visit epileptiform attacks of a grand mal nature developed. They have been controlled by medication. During the past two years there has been some thinning of the left side of the face, with the reappearance of some fat on the right side, so that the two sides are now nearly symmetrical. It is difficult to say whether this is a case of true facial hemiplegia or localized lipodystrophy or one of a hypothalamic disturbance involving the central nervous system.

CASE 2.—This 5 year old boy was brought for examination about eight months ago because the left side of the face had become much smaller than the right during the previous eight or ten weeks. The skin on this side feels hard and leathery and is immovable. There are obviously little or no fat present and little or no evidence of muscular weakness. The oral mucous membrane is pale. On the left side of the nose, extending onto the maxillary area and the neck, are light yellow, shiny areas. At the beginning they were slightly edematous. These areas suggest scleroderma, although the department for diseases of the skin does not consider them typical of this condition. A good reason for considering scleroderma is the close association between this condition and facial hemiatrophy. Some authors speak of facial hemiatrophy as a complication of scleroderma. Roentgenograms and measurements carefully taken at the University of Illinois School of Dentistry reveal no evidence of bony change. There has been no sensory change. The results of neurologic examination are otherwise negative. This case looks like a typical instance of facial hemiatrophy.

CASE 3.—This white boy, aged 9, shows an unusual type of progressive disease of the central nervous system. Three conditions are spoken of as belonging to the same group: neurofibromatosis, tuberous sclerosis and hematomas of the brain with nevi on the skin. This is a typical case of sclerosis tuberosa. The patient has warty, sebaceous-like lesions chiefly on the nose but spreading out over the face, epileptic attacks of the grand mal type and amentia. These patients often show other congenital defects of various kinds. This boy also has very defective vision. There is no optic atrophy, as is sometimes found in such cases.

ACTINOMYCOSIS (PULMONARY). DR. EUGENE T. MCENERY.

This case was presented as one of pulmonary actinomycosis about one and a half years ago at the Central States Pediatric Society. The patient was first seen in the hospital in February 1932 because of a persistent cough of five months' duration, loss of weight and a painful swelling on the chest which had developed in the previous month. He has never been out of Chicago and has always lived on the southwest part of the city, thus having little opportunity to come in contact with grain or cattle. Examination revealed a thin boy with a large indurated swelling on the wall of the left side of the chest along the border of the sternum. This mass was aspirated, and typical sulphur granules of actinomycosis were identified. Roentgenographic examination revealed marked infiltration throughout the entire left lung. A year later this state of affairs existed. (Lantern slides were shown.) The large mass was incised and curetted. The patient was given increasing doses of a saturated solution of potassium iodide, beginning with 30 drops (1.8 cc.) three times a day. This was increased gradually until he was taking 300 drops (18.5 cc.) a day and was continued for ten months. No signs of iodism appeared during this period except for occasional spells of vomiting after meals. The dosage was decreased, and now he is taking 90 drops (5.5 cc.) a day. A year after the original mass appeared a similar swelling developed in the same place; this was drained, and since that time he has had no recurrence.

In a review of the literature no patient with pulmonary actinomycosis has survived more than two years. This boy has been followed for three years, and at this time the results of physical and roentgen examination are normal (a lantern slide was shown).

EMPYEMA. DR. EUGENE T. MCENERY.

The next group of patients are those with empyema following pneumonia. Because we have reported many cases in which the patients were treated by aspiration alone, some of our friends think that this is the only method used here. This group were in the hospital about one year ago and were treated by surgical drainage. The motion picture shows how we follow up the patients with physical therapy, deep breathing exercises and getting them up and about as soon as possible in order to lessen the thoracic deformity and reexpand the lung. (Motion pictures were shown.)

DIABETES MELLITUS. DR. ALVAH NEWCOMB.

In December 1932 a boy was admitted to the hospital in a deep diabetic coma. He was given 200 units of insulin and fluids subcutaneously, but expired in three hours.

My associates and I were looking for some better method of treatment. This year a boy, aged 8, was admitted in almost as serious a condition as the former patient. We had heard of lactate Ringer's solution (as devised by Hartmann) but had none on hand and began treatment by the old method. Within two hours the child was worse. After the solution arrived, it was administered; the patient revived rapidly and recovered nicely. We have had four other cases in which we used this solution.

This boy, aged 9, was brought in because of listlessness for four days, abdominal pain accompanied by nausea but no vomiting of two days' duration and a history of measles about two weeks before the onset, with glycosuria for five months. On admission he was stuporous; the respiratory movements were very slow; the blood sugar was 317 mg. per hundred cubic centimeters, and the carbon dioxide-combining power of the blood plasma was 10 volumes per cent. He also had lipemia, which one sometimes finds in patients on a diet in which carbohydrates have been restricted.

When the carbon dioxide-combining power was reported, a continuous intravenous drip of sodium lactate was begun, with 60 units of insulin. The amount of sodium lactate was calculated according to Hartmann's formula, and in this case was 1,900 cc. Within four hours the patient received this amount intravenously. This treatment was begun at 3:30 p. m., and by 4:40 the patient was much improved and the pain in the abdomen had subsided. At 8:00 p. m. he was normal in most respects clinically, but there were a great deal of diacetic acid in the urine and some dextrose. At midnight there was still some sugar in the urine. By 4:00 a. m., twelve hours after treatment was begun, the urine was free from sugar. The following day he was placed on almost the full diet.

The advantage of the method devised by Hartmann (who has used the intravenous drip in severe cases of diabetes mellitus) is that it can be used anywhere, and if one figures up by one method of calculation the amount of sodium lactate needed to raise the carbon dioxide-combining power from 10 to 35 volumes per cent one can give 60 cc. of the solution per kilogram of body weight. It is a rapid yet safe method of clearing up ketosis, glycosuria and hyperglycemia.

Furthermore, with this method one can definitely tell the amount of fluid that is absorbed, while when fluids are given subcutaneously the absorption is often poor, and if the patient is taking fluids by mouth one is at a loss to determine the amount absorbed after vomiting. The improvement in the circulatory system is rapid: The pulse becomes fuller and slower; a pink color returns to the face, and the sensorium rapidly clears.

SPONDYLOLISTHESIS. DR. FREMONT A. CHANDLER.

Backache ranks first or second among the complaints of adults coming to a general clinic. In children this occurs much less frequently than in adults. One of the most common causes of this symptom in adults is spondylolisthesis in its various grades. This condition was first considered of importance by the obstetrician in its relation to childbirth in the middle of the nineteenth century. However it had not been recognized in children. More recently it has been found to be fully as prevalent in males as in females, and during the last few years examples of this condition have been observed in children.

The lumbosacral juncture of the spine has become an especially vulnerable area because of the assumption of the upright position and the failure of nature to adapt this part of the spine to the resulting increase of weight. The surface of the sacrum presents an inclined plane on which the superimposed weight tends to slip off anteriorly. Such slipping is prevented by the overhanging of the inferior articular processes, which hook over the posterior aspect of the first sacral surface. If this bony check has been lost anterior slipping results, with a gradual stretching of the ligamentous and muscular tissues of this area.

Separation of the posterior arch of the last lumbar vertebra is of frequent occurrence, and because of this anterior migration of the fifth lumbar vertebra is not uncommon. The fact that the soft tissues are poorly adapted for bearing weight results in painful symptoms in this area.

Eight cases of spondylolisthesis occurring in patients between the ages of 6 and 15 are presented; all these patients have distinct histories of severe falls which resulted in immediate disability of the back. Four have been operated on, and the loose posterior segment of the last lumbar arch was found. Transplantation of the tibial cortex to this area resulted in a satisfactory outcome and the relief of the symptoms in each case.

The most characteristic diagnostic sign was the presence of a hard, bony tumor, located in the midline at the level of the fifth lumbar vertebra. This tumor was found to consist of the spinous process of the detached segment, which remained in its proper relation to the sacrum, whereas the body of the fifth lumbar vertebra and the superimposed spinal column had advanced forward.

(This presentation was accomplished by demonstrations on models and by slides showing the pathologic changes, mechanism and clinical features.)

PRESACRAL TUMOR: TERATOMA. DR. ALBERT H. MONTGOMERY.

Dr. Brennemann asked me to tell the members about a tumor which I saw in a girl 11 months of age whom he referred to me.

The tumor, the size of a large orange, was located in the right buttock near the upper portion of the gluteal fold. It rested between the coccyx and the rectum and moved up and down slightly with respiration. It was painless and was producing no symptoms when my associates and I saw the child. It had grown steadily since birth.

The question of diagnosis was interesting. We had seen several patients in the last few years with presacral tumors, and the possibility of a chordoma was suggested, because that tumor was present in three of the cases. However, those tumors are usually associated with some urinary or rectal trouble, and this patient had no such symptoms. There was also the probability of a dermoid to be considered. Careful pelvic examination failed to show anything that would suggest a uterine or adnexal tumor.

At operation a large transverse incision was made just below the coccyx, and a large encapsulated tumor with a well established blood supply was encountered. During isolation of the blood vessels the capsule was opened and the tumor incised. It was found to contain two loops of bowel with a definite mesentery. This made me think I was in the abdomen, but a little investigation showed that both the loops had blind ends, so evidently the tumor was a teratoma. Complete removal of the tumor was difficult because of the immediate proximity of the blood supply

of the rectum, but it was finally accomplished without any mishap. After the wound was closed the child was kept lying on her face for a week, and primary healing was secured.

When the tumor was examined carefully after removal it was found to contain a fallopian tube, a renal pelvis, gastric mucosa and adrenal tissue, in addition to two small loops of bowel, all embedded in coarse fatty tissue enclosed in a firm capsule. The specimen which is being passed around shows the structures in the center of the tumor mass.

Tumors of this character, which are not infrequently located in the presacral region, range from the dermoids, which often contain hair, nails and other epithelial structures embedded in sebaceous material, to the teratoid tumors, which contain bone, cartilage and other cells but which have no definite structure. Still further advanced are the teratomas, as in this case, which are made up of a bizarre mixture of portions of various organs, and, finally, the so-called fetal inclusions, which may vary from a monstrous tumor formation to a Siamese twin.

Several years ago I operated on a child who had what appeared to be something like a tail. This was a pear-shaped tumor that came off the posterior portion of the sacrum but had no connection with the spinal column. When the tumor was dissected a well formed embryonic right scapula was found in the center of a large mass of coarse fatty tissue. Teratomas are probably due to misplaced germinal layers, and as they contain finished structures they are probably bigerminal rather than monogerminal.

"Meningococcia" (Meningococcic Infection): A New Remedy. Dr. Archibald L. Hoyne.

The term "meningococcia" is suggested for all classes of meningococcic infection with or without evidence of meningitis. Under meningococcia are included: (1) meningococcic meningitis; (2) meningococcemia; (3) meningococcemia with meningitis and (4) meningococcus carriers.

Of fourteen patients suffering from meningococcic meningitis at the Children's Memorial Hospital, eight were treated with Ferry's meningococcus antitoxin alone; three received standard antimeningococcic serum and three, who were first treated with standard serum and did not respond, were given antitoxin in addition to serum. There were but two deaths, both occurring in patients who had been treated with antitoxin, making a fatality rate of 14.28 per cent.

Patients should receive the first treatment of serum or antitoxin intravenously; the dosage is 100 cc. for an adult, and 50 cc. for a child, diluted with at least an equal volume of 10 per cent solution of dextrose. In severe cases intravenous treatment may be repeated.

The usual high fatality rate for meningococcic meningitis can be greatly reduced by the intravenous use of either antimeningococcic serum or meningococcus antitoxin. The value of the antimeningococcic serum is due to whatever amount of antitoxin it may happen to contain. The Ferry meningococcus antitoxin seems to be far superior to any antiserum now available.

Lumbar puncture is not required in certain cases of meningococcemia, and eventually intrathecal therapy may prove to be entirely unnecessary.

Lead Poisoning. Dr. Jack Chesney.

I am sorry that we are unable to present our patient, but he contracted measles recently and is still in quarantine.

The patient is a 2 year old white boy who was admitted to the hospital on Oct. 4, 1934, having had a generalized convulsion about one hour before admission. It was stated that he became ill about three months previously and began to have repeated attacks of projectile vomiting associated with diarrhea. These attacks lasted for three or four days; he was well for a week or more and then had another attack. About a month before admission he had a generalized convulsion that lasted twenty minutes or more, from which he recovered without difficulty. The

evening of his admission the child became unconscious and had twitching of the face and movements of the arms and legs; he was brought to the hospital just at the termination of the convulsion. On inquiry the mother stated that the child had eaten a considerable amount of plaster during the summer.

Examination showed a moderately well developed child, somewhat dehydrated and in a comatose state. He could not be aroused even on examination of the ears. There was no generalized glandular enlargement. The head was rather large, and the veins of the scalp more prominent than normal. The fontanels were open. Macewen's sign was elicited on tapping the skull. The pupils were moderately dilated and reacted sluggishly to light. There was papilledema of at least 2 diopters. The veins were enlarged and tortuous; there was no evidence of exudate or hemorrhage in the eyegrounds. The mouth was normal, but three teeth were missing. This the mother explained by stating that the child had fallen from his crib three months before and knocked out these teeth. The child appeared to have generalized hypotonia. The knee reflexes were not obtained. There was slight stiffness of the neck, but there was no Babinski reflex, and the Kernig sign was negative.

On the basis of the history and the physical findings on admission our impression was that the child had an intracranial tumor, and that the convulsions were probably associated with this tumor. Examination of the blood showed a normal red cell count and hemoglobin. Later we thought that this was due to the fact that the child was dehydrated, for the red cells showed anisocytosis and poikilocytosis. The urine showed acetone and diacetic acid. The Wassermann reaction and tuberculin reactions were negative.

On the morning following admission the child sat up in bed and ate his breakfast normally. The positive Macewen sign, stiffness of the neck and changes of the eyegrounds were still present, and there was a considerable amount of hypotonia. He had the typical staggering gait of cerebellar disease. He was seen by Dr. Brennemann that day, who thought that the child probably had a tumor in the cerebellar midline. He called in Dr. Bucy, who concurred in this diagnosis and went so far as to suggest that the tumor was probably a medulloblastoma. A roentgenogram of the skull showed rather marked separation of all the sutures. The sella turcica seemed entirely normal, and there was no evidence of digitations of the skull as seen in brain tumor. The child was observed for about four days, during which the respiratory rate, temperature and pulse rate became normal. He vomited at least once every two days, and the nurses stated that he cried out at night as though he had a headache.

The child was transferred to the Albert Merritt Billings Hospital on October 8. On October 11 Dr. Bucy performed a craniotomy, using the cerebellar approach. He found no tumor in the region of the cerebellum but carried out a decompression. The child was brought back to the ward in good condition, and following this operation the swelling of the disks disappeared.

The fact that the child had eaten a considerable amount of plaster during the summer was entirely overlooked, and on further questioning the mother stated that the child had also eaten some paint. Examination of the blood showed no stipple cells, but roentgenograms showed the typical findings of lead poisoning. On spinal puncture 66 cc. of spinal fluid was obtained and 0.025 mg. of lead found; 700 cc. of urine contained 0.1 mg. of lead. This was two to three times the so-called highest limit of normal as reported by investigators. Blood was taken on October 29 and sent to Bloomberg of Johns Hopkins University, who found 0.2 mg. of lead in each hundred cubic centimeters. One month later there was 0.1 mg. of lead per hundred cubic centimeters of blood.

Since that time the child has improved, and at present the results of neurologic examination are entirely negative, but a small fluctuant tumor is still present over the area of exploration. The lead line is now almost a double line, as seen in the picture. The patient was given phosphanized cod liver oil over a period of about three months.

DERMAL SINUS (CONGENITAL). DR. DOUGLAS N. BUCHANAN.

CASE 1.—L. I., a white girl, aged 5, was admitted to the Children's Memorial Hospital in November 1932 because of pain in the neck and back.

From her birth her parents had noted a small dimple in the midline of the upper portion of the back. In all other respects the child seemed normal. At 6 months of age the site of the dimple became swollen and purple and discharged a slightly bloody material. At this time she had fever, sore throat and a rigid back, and a physician found 150 cells in the spinal fluid. A pellicle formed on this fluid, and a portion was injected into a guinea-pig. This animal died three weeks later and is said to have shown evidence of tuberculous disease on post-mortem examination. Another specimen of spinal fluid was injected into a second guinea-pig, and this animal died also. This was regarded as conclusive proof that the child was suffering from tuberculous meningitis. This illness continued with varying degrees of intensity for eighteen months, when the child spontaneously recovered and remained well until 5 years of age.

Examination at the time of admission showed spasm of the left sternomastoid muscle; scoliosis of the upper thoracic vertebrae, with the convexity to the right, and a small dimple just above the spine of the fifth thoracic vertebra. Both the knee and the ankle jerks were increased, and sustained ankle clonus was present bilaterally. The right plantar response was extensor and the left, flexor. A roentgenogram showed incomplete fusion of the laminae of the fourth thoracic vertebra and marked spinal curvature. The patient improved and was discharged after ten days. During the succeeding months she became more spastic, and the reflexes in her legs were more active. She was readmitted to the hospital on April 22, 1933 for lumbar puncture. The cerebrospinal fluid was clear and colorless, contained 3 lymphocytes per cubic millimeter and gave a negative Pandy reaction.

In June she began to scratch and rub the ulnar surfaces of both hands and both arms, presumably because of paresthesias. She was again admitted to the hospital. On lumbar puncture a yellow fluid was obtained under very low pressure, and Queckenstedt's test showed evidence of a partial block in the spinal subarachnoid space.

On August 10 she was transferred to the Bobs Roberts Memorial Hospital for Children of the University of Chicago Clinics for exploratory laminectomy. Neurologic examination at that time showed no defect in the cranial nerves. The deep reflexes in the arms were normal; those in the legs were much increased. A sustained ankle clonus was present on the right side and a transient clonus on the left. Both plantar responses were extensor. No definite sensory level could be demonstrated. There was no localized atrophy in any group of muscles, but in general the strength was poor. The legs showed extensor rgidity, and the gait was spastic. Lumbar puncture at this time showed clear fluid with no cells, and there was evidence of a partial block.

On August 16 laminectomy was performed on the third, fourth and fifth thoracic vertebrae. The spine of the fourth thoracic vertebra was absent. The dimple was found to be continuous with a stalk of tissue about 3 mm. in diameter which contained a central canal filled with thick caseous material. The stalk extended from the dimple downward through the posterior spinal muscles, through the defect in the laminae of the fourth thoracic vertebra to the dura mater, to which it was firmly attached. Beneath the dura at this point a firm mass was palpable, which was cut off from the posterior surface of the cord. Within the mass there were numerous cystic spaces containing thick sterile pus.

By December the patient was able to walk and run without any sign of spasticity or limp. The deep reflexes of the legs were brisk, and the plantar responses were extensor.

Pathologist examination of the specimen removed showed it to consist of a tube of epithelial tissue opening out on the surface of the skin at the dimple and extending downward to the mass lying beneath the dura mater. This mass was closely attached to the posterior surface of the spinal cord.

The tube was lined with epithelium which, however, was defective at the point of contact with the dura mater. The fibrous mass at the bottom of the tube was mainly a thick feltwork of connective tissue containing numerous sterile abscesses, involving the arachnoid and attached to the posterior surface of the spinal cord.

This congenital malformation is identical with the pilonidal sinuses which occur in the sacral and coccygeal regions. It is possible to interpret the patient's symptoms once the condition is known, and it is obvious that she suffered from recurrent infections of this congenital defect, each attack increasing the size of the fibrous tissue mass until compression produced the signs and symptoms of paraplegia.

CASE 2.—J. S., a white girl, aged 3, was admitted to the Children's Memorial Hospital in September 1933, complaining of pain and stiffness of the back, difficulty in walking and itching and painful feet. These symptoms and signs had been present for four months.

Her birth and development had been normal, but a small hairy mole over the fourth lumbar spine had been noticed since birth.

General physical examination gave normal results, and spinal puncture on two occasions showed 700 and 680 cells, 83 and 32 per cent, respectively, of which were lymphocytes. Culture of the first specimen showed Bacillus proteus, but the second specimen was sterile. Tuberculous meningitis was suggested as the most probable diagnosis. The child, however, was removed from the hospital and was brought back in January 1934, complaining of pain when the legs and feet were moved, weakness of the legs and paresthesias in the left foot.

Neurologic examination showed that the cranial nerves were normal. The knee and ankle jerks were absent on both sides; both plantar responses were flexor; there was extreme weakness of the peroneal group of muscles of the left leg, and no gross sensory change could be detected.

She was admitted to the Bobs Roberts Memorial Hospital for Children of the University of Chicago Clinics in March for exploratory laminectomy. Seven days before admission her left leg had become completely paralyzed and she had incontinence of feces and retention of urine, with overflow incontinence. The only change in physical signs obtained at that time was that the left leg was completely paralyzed except for slight movement at the ankle and toes.

A roentgenogram of the spine showed incomplete fusion of the laminae of the sacral segments. Lumbar puncture was made between the fifth lumbar and the first sacral spine and thick caseous pus encountered. Some of this fluid was aspirated, and on culture Bacillus coli was grown.

At operation an incision was made in the midline from the eleventh thoracic to the first sacral spine, the reddened nevus being excised. From the center of the nevus a small white fibrous tube passed down between the spines of the fourth and fifth lumbar vertebrae to the dura, to which it was firmly attached. On incision of the dura an abscess was exposed, extending from the fifth lumbar to the twelfth thoracic vertebra. This was evacuated, and drains were left in situ for four days.

When last seen, on May 29, the patient was able to walk without assistance, although there were some external rotation and eversion of the left foot.

Pathologically, the condition was essentially similar to that seen in the first patient, although the abscess cavity was much larger and the sinus could be traced down through the dura. The other essential difference was that in the second case the sinus passed between intact vertebral arches instead of through a defect in the laminae.

SUPRASELLAR CRANIOPHARYNGIOMA. DR. DOUGLAS N. BUCHANAN.

L. L., a white girl, aged 9, was admitted to the Children's Memorial Hospital on March 11, 1935 with a complaint of defective eyesight for three weeks. Birth and early development had been normal. In November 1934 she had an infection of the upper respiratory tract, and from that time until admission she suffered from

severe headache. On Jan. 1, 1935 her left eye turned inward and remained so for three weeks. Since January 1935 she has had attacks of vomiting every seven days. Her breasts enlarged at the age of 7, and axillary and pubic hair has been present for six months. There has been no menstruation.

On examination the patient showed secondary sexual development. Percussion of the skull produced Macewen's sign of increased intracranial pressure. Both fundi showed disks which were elevated to 2 diopters. The visual fields showed a restriction of the right field of 15 degrees and a restriction of the left field of 20 degrees. There was a suggestion of binasal hemianopia. Visual acuity was 20/40 in the right eye and 2/200 in the left. Both pupils were central, regular and circular; they reacted slowly to light, and the reaction was through a small range and was not well held. The conjugate movements of the eyes were full in all directions. There was no limitation of upward movement in either eye on voluntary effort or on Bell's maneuver. There were no nystagmus in any direction, no ptosis, no exophthalmos and no strabismus. The corneal reflexes were present and normal on both sides. There was a slight weakness of the left lower side of the face. The rest of the cranial nerves were normal. The deep reflexes were symmetrical and normal. The plantar responses were flexor on both sides. There was no clonus. The motor system showed no local weakness or atrophy, and there was no abnormality of sensory appreciation on any part of the body. There were a fine terminal ataxia and tremor in the fingers of both hands during movement.

Laboratory examination of the blood and urine showed no abnormality. The dextrose tolerance test showed the following values for the blood sugar: during fasting, 91 mg.; one-half hour after a meal, 174 mg.; one hour after a meal, 190 mg.; two hours after a meal, 118 mg., and three hours after a meal, 94 mg. A roentgenogram of the wrist showed no evidence of a lead line. A roentgenogram of the skull showed slight diastasis of the sutures and an intracranial calcification above the sella turcica and behind the anterior clinoid processes.

The child shows the clinical and roentgenographic signs of a suprasellar craniopharyngioma, and in addition she has the uncommon features of unusually early secondary sexual development.

SUMMARY OF A SOCIAL STUDY OF FIFTY-NINE SPASTIC CHILDREN. CAROLINE HUBERT ELLEDGE.

A study of fifty-nine spastic children was made by the social worker in the orthopedic clinic at the Children's Memorial Hospital. It was found that most of the children improved physically with surgical intervention and physical and occupational therapy. More than one half of the group had defective vision, and about one third had serious defects of speech.

Contrary to the general opinion that a spastic person is necessarily mentally defective, the study indicated that twenty-two of the fifty-nine children rate as average or above average in mentality. There seemed to be no correlation between the extent of the physical handicap and mental ability. For example, there were two persons of the genius class in the group—one a patient with mild hemiplegia, the other a patient with serious paraplegia. The school performance of several of the so-called dull patients or those with borderline mentality refuted the reliability of the scores which they received on the intelligence tests. It was pointed out that the emotional, environmental and physical make-up of the spastic child often prevents a true interpretation of his mental ability. The caution was extended, therefore, to weigh all factors carefully before committing a supposedly feebleminded spastic child to a state institution. There were many children in this group who greatly improved in personality and mental response after physical, social and educational treatment.

It was demonstrated that the conditions in the home of the spastic child are an important factor in the development of his personality. The parental attitudes of despair and discouragement are quickly taken up by the child. As this type

of child is all too soon aware of the marked contrast that he presents to the normal person, a discouraging parental attitude increases his emotional instability and lack of self-confidence. If the parents are hopeful for his future and encourage him, he usually responds more quickly to the educational and social program created for him by the community. The case of Dr. Carlson of New York was cited as that of a person with severe spasticity who, through his own efforts and a sympathetic environment, has sufficiently overcome his handicap to definitely take his place in the world.

SALICYLATE POISONING. DR. CHARLES SCHOTT.

About a year ago a child was brought on the wards when Dr. Brennemann and I were making rounds. The child seemed very ill, had hyperpnea and was flushed and unhappy. The mother, who had had experience in hospitals, had brought in a morning specimen of urine. This was rushed to the laboratory, and the sugar reaction was reported. The child was given some insulin and dextrose. The mother stated that in the hospital from which she took him they had given him injections of salicylate by rectum.

Recently I sent a child with rheumatism to the hospital and advised mild doses of salicylate. I had to leave town, and when I came back two days later the intern called me up and told me that the child had encephalitis. He said that on the previous afternoon the child became drowsy and showed hyperpnea, and that he was called and told that the child was bleeding from the rectum and vomiting blood. I went to the hospital in the morning and found that the child had been getting about from 14 to 15 grains (0.9 to 0.97 Gm.) of salicylate, and that this dose had suddenly been increased to 100 grains (6.5 Gm.). This was the cause of his "encephalitis." He bled so much that the hemoglobin dropped from approximately 100 per cent to 48 per cent in two days. He was passing pure blood from the rectum and vomiting pure blood. All treatment was stopped except alkalinization. In these cases of salicylate poisoning dextrose does no good. Alkalinization seems to be the treatment that helps.

I am bringing this to the attention of the members because we are living in an era of high salicylates, and it is important to know what the picture of salicylate poisoning is so that one can rule out encephalitis, gastric ulcer or intestinal hemorrhage.

DICK TEST. DR. MANDEL L. SPIVEK.

This paper will be published in full in a later issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

HEMANGIOMA OF THE SKULL. DR. WILLIAM E. ANSPACH.

Benign vascular tumors of the soft tissues are easily recognized, but hemangiomas involving bone are less seldom seen and are seldom diagnosed correctly. This is especially true of hemangioma of flat bones, which has brought about a number of reports of cases in which the growth had been diagnosed as a malignant tumor.

F. S., a girl, aged 11, was in the Children's Memorial Hospital in 1921 because of a tumor-like mass in the left side of the skull, which was thought to be an osteogenic sarcoma. An operation was attempted, but the patient had a terrific hemorrhage on the table, and the operation was not completed. Various kinds of treatments were necessary for several days to control the hemorrhage. The patient finally recovered and left the hospital. A roentgenogram at the time of admission to the hospital showed a "sunray" pattern of bony trabeculation within the tumor.

The patient did not return for roentgenotherapy in 1921; the family moved, and she was lost trace of until located recently by our social service department. She is now 26 years old and the mother of a 2 year old child. She has enjoyed perfect health since leaving the hospital fourteen years ago. Roentgenograms made at

this time show that the tumor approximately one third larger and the bony trabeculation is made up of radiating spicules of denser bone. This increase in proportion of bone to soft tissue has been brought about in another patient (an adult) by roentgenotherapy in a comparatively short time.

This case is of interest not only because of the long period of observation but because it emphasizes the diagnostic importance of roentgenograms in these cases. The most perfect example of a sunray tumor with trabeculation reaching to the site of origin is produced by hemangioma of flat bone and should not lead to a diagnosis of a malignant osteogenic sarcoma.

CHICAGO PEDIATRIC SOCIETY AND CHICAGO GYNECOLOGICAL SOCIETY

Joint Meeting, April 19, 1935

STANLEY GIBSON, M.D., *President, in the Chair*

CEREBRAL HEMORRHAGE IN THE NEW-BORN. DR. A. LEVINSON.

Cerebral hemorrhage occurs more frequently in prematurely born infants than in infants born at full term. In only 0.45 per cent of the infants in our series born at full term was the diagnosis of cerebral hemorrhage made, whereas 19.1 per cent of the prematurely born infants studied had cerebral hemorrhage.

Prematurity is the most important cause of cerebral hemorrhage in the newborn—a fact which is substantiated by both clinical observations and observations at necropsy.

Cerebral hemorrhage varies in location and extent, the most frequent site of hemorrhage being the subarachnoid space. Meningeal hemorrhage was present in all our cases irrespective of involvement of any other part.

There are undoubtedly cases of cerebral hemorrhage with no other symptoms; these are cases in which the hemorrhage is very slight. There are also cases with no symptoms during the neonatal period, but in which later, at 6 months or more, the first symptoms, such as inability to sit up or signs of idiocy, appear.

The symptoms during the neonatal period are of two types: irritative and somnolent. Some infants exhibit a combination of the two types. The irritative type is characterized by great restlessness, a high-pitched cerebral cry, moaning and a pained expression; the anterior fontanel usually bulges. The somnolent type, which is most frequent in prematurely born infants, is charactertized by apathy, subnormal temperature, difficulty in swallowing and sometimes a depressed fontanel. Because such infants do not take food well they become dehydrated very rapidly.

We believe that bloody cerebrospinal fluid is not diagnostic of cerebral hemorrhage, since it may be due to trauma from puncture, nor does clear cerebrospinal fluid entirely exclude a diagnosis of cerebral hemorrhage. Of greater value in diagnosis is xanthochromia with a positive reaction to the benzidine test and an increase in the amount and pressure of the cerebrospinal fluid.

The most important element in the treatment of cerebral hemorrhage is complete rest. Should the patient have convulsions sedatives may be administered rectally. The increased intracranial pressure may be relieved by the intramuscular introduction of hypertonic solutions of sodium chloride or a 10 to 15 per cent solution of dextrose.

Spinal puncture is indicated in the irritative type when there are convulsions and constant moaning, but has no therapeutic indication in the somnolent type.

Should the theory that nature sometimes brings about absorption of the meningeal hemorrhage without leaving a scar be true, a brighter outlook is afforded patients suffering from cerebral hemorrhage.

CARE OF THE NEW-BORN FROM THE STANDPOINT OF THE PEDIATRICIAN. DR. ISAAC A. ABT.

The new-born infant should be put to the breast once in the first twenty-four hours and should, if possible, empty the breast before artificial feeding is begun. A 5 per cent solution of lactose or dextrose may be given during inanition. Fever and dehydration should suggest transitory or thirst fever. Fluids should be increased by mouth or, if necessary, by hypodermoclysis.

If the baby is deeply asphyxiated at birth it is unwise to use artificial respiration until cardiac function is in action or restored. The infant should be kept quiet and warm; baths and bodily movement should be avoided because of the danger of increasing the cerebral hemorrhage which may have occurred. Asphyxia may be treated by the inhalation of oxygen or oxygen with carbonic acid. Henderson recommended 7 per cent carbonic acid with oxygen. This may be administered with an anesthesia mask or by intratracheal insufflation. The Drinker respirator may be employed, although the inhalation method is less violent.

Convulsions constitute an ominous symptom in the new-born, and one should suspect an organic lesion of the central nervous system. Premature infants are exquisitely predisposed to hemorrhage and convulsion.

Meningitis in the new-born is difficult to diagnose. The ordinary signs are usually absent, and convulsions and fever are the only symptoms. Lumbar puncture is commonly necessary for diagnosis. Convulsions may occur in cases of dehydration or may be caused by encephalitis. In cases of cerebral hemorrhage convulsions sometimes cease for several days; the child seems to progress normally, but in a year or two motor or physic disturbances are noted as a result of the original hemorrhage. Tetany in the new-born is very rare, but may be observed as early as the second month. Children of eclamptic mothers may have convulsions. Adrenal apoplexy with convulsions is usually not diagnosed during life.

Nearly every mother can and should nurse her baby. The contraindications are: (1) A tuberculous mother. This constitutes danger to the baby and also to the mother, for the tuberculous process may be activated during lactation. (2) Severe chronic disease of the mother—nephritis, diabetes, debilitating disease, recurrent epilepsy, organic nervous disease or psychic disturbances. Nursing during an acute infectious disease of the mother is impractical. If a child is nursed during mastitis there is danger that micro-organisms or pus may be introduced into the milk. Pain during nursing makes nursing intolerable to the mother.

The influence of diet on the maternal milk supply is slight. Salads, cabbage and raw fruit do not affect the milk. The mother should take one-half again as much food as she was in the habit of taking before nursing the child. She will get the required amount of food by consuming at least a quart of milk and three good meals. Some drugs are excreted in milk, mostly in small quantities. Sucking the breast is the best stimulant to the flow of milk. A healthy psychic condition of the mother with joy and a will to nurse is not the least important factor.

Icterus may occur, and the cause may be in the liver or the blood. If it is in the liver, bilirubin is found in the urine; if in the blood, there is no biliary pigment in the urine. A differential diagnosis should be made between neonatal icterus, septic icterus, icterus gravis, icterus due to congenital malformation and to atresia of the bile ducts and syphilitic icterus. Icterus gravis appears on the first day; neonatal icterus, on the second or third day. The spleen is enlarged in icterus gravus; occasionally an infant with this disorder recovers. Septic icterus occurs in the new-born and in older nurslings and may be secondary to umbilical infection, pneumonia or another focus of infection. Icterus due to atresia of the bile ducts may cause symptoms in several days or a week or more after birth. The stools are acholic; the urine is dark and gives a reaction for bile pigment. The liver and spleen are enlarged; ascites develops, and the disease results fatally within a few months. The symptoms of syphilitic icterus resemble those which occur in cases of atresia of the bile ducts and may be the only signs of congenital syphilis.

The liver and spleen are enlarged in cases of syphilis, though there may be diffuse syphilitic disease of the liver without jaundice.

INJURY AT BIRTH: PREVENTION AND RESULTING MORTALITY FROM THE STANDPOINT OF THE OBSTETRICIAN. DR. CHARLES E. GALLOWAY.

At the Evanston Hospital investigation of the last 5,000 deliveries reveals the fact that there were fifty-one major injuries, including fatal cerebral hemorrhage. Besides these there were thirty-seven minor injuries, including abrasions from a forceps and other contusions of minor importance. At the same hospital an analysis of the autopsies on fetuses for the last ten years showed that 34 per cent of the deaths of fetuses, including premature babies, were due to cerebral hemorrhage. It also shows that 40.6 per cent of the autopsies on babies born at full term who died at birth demonstrated cerebral hemorrhage.

The precise manner in which the tentorium or other intracranial structures are torn does not seem to be important. About all that is known concerning the etiology of cerebral hemorrhage can be summed up in four statements: 1. Distortion of the head causes the underlying sinuses to be partially compressed, with resulting disturbances of the intracranial circulation of blood. 2. Compression of the head in one direction causes a compensatory elongation in other directions, and this strain is most marked along the free edges of the tentorium. 3. Negative pressure causes a suction effect on the presenting part of the head in vertex presentation and on the uppermost part of the head in breech presentation. 4. The character or strength of the tissue put under stress is an important determining factor.

The use of an outlet forceps in conjunction with episiotomy will probably result in fewer cerebral hemorrhages. If a forceps is used, it is much less dangerous to make a cephalic application than a pelvic application, and it is also essential that there be no squeezing with the blades. If necessary, a towel or set-screw should be used to prevent such squeezing when effort to extract the head is exerted.

After a long labor in which molding of the head has occurred to a marked degree, such a molded head should be released quite slowly.

Another contributing cause of cerebral hemorrhage is a violent attempt to resuscitate the baby, especially Schultze's swinging.

Many obstetricians give the baby an injection of 20 cc. of whole blood in the thigh as a routine following all difficult deliveries. It is thought that this procedure lowers the coagulation time and thereby helps to prevent what would become a dangerous hemorrhage from a point where slow oozing is occurring.

Another contributing cause of cerebral hemorrhage and one which is probably considered by most obstetricians is a too prolonged test of labor. Since cesarean section now carries a satisfactorily low risk, it behooves the obstetrician to use it oftener in cases in which the pelvis is known to be abnormally flat or small rather than to allow a cerebral hemorrhage to develop in the baby in an attempt to see whether the uterine contractions can force the head through the inlet.

In this study of 5,000 deliveries there were 222 cesarean sections. Two babies showed symptoms of cerebral irritation but recovered and were discharged apparently well. Both had had a test of labor. Two other babies were cut with the scalpel on opening of the lower uterine segment. These were the only injuries among this group of 222.

The same can be said of the second stage of labor with the head deeply engaged. Delivery should be effected with episiotomy and a forceps generally within two hours. Further delay only tends to raise the mortality.

There were only 4 cases of injury of the brachial plexus in this series of 5,000 deliveries, and they were all quite mild. The symptoms lasted only from a few hours to a few days. Three of the infants were delivered with a forceps, and one was born spontaneously.

In this series there were only fourteen fractured clavicles, giving an incidence of 0.28 per cent. The relative number of fractured clavicles in cases of breech presentations seems to be much higher than in those of vertex presentations.

Wryneck noticed at birth is a true congenital anomaly in practically all cases. Trauma as the cause is very exceptional. The pathologic state of the sternocleidomastoid muscle is probably due to an anomalous attitude of the head, and this faulty attitude may favor presentation by the breech. Comparatively slight traction suffices to lacerate this abnormal muscle, but the laceration may even improve its condition.

Breech delivery and version with breech extraction show a higher incidence of injury at birth than any other type of delivery. The fetal mortality is also correspondingly high.

Several pertinent facts should be mentioned relative to breech extraction. The unnecessary haste displayed by the average operator seems most objectionable, and the next most undesirable factor is the lack of complete relaxation and dilatation of the soft parts. Breech extraction calls for complete dilatation and deep ether anesthesia. Episiotomy is called for in practically every case.

During breech extraction the operator should avoid pressure on the fundus, extreme angulation, excessive suprapubic pressure and dangerous traction. It is possible to elongate the spinal column about 5 cm., and the thoracic portion of the cord of the fetus is only about ⅛ inch (0.32 cm.) in diameter. The cord is enlarged in the cervical and lumbar region and is well anchored by the brachial plexus above and the cauda equina below. It is for these reasons that extreme traction causes injury of the thoracic portion of the cord in some cases.

DISCUSSION

DR. M. L. BLATT: The vital statistics for the city of Chicago for the year 1934 record the deaths of 700 infants from "prematurity." This audience, composed of obstetricians and pediatricians, is interested in this fact. If these figures are to be reduced during 1935 it will be through the individual efforts of those present.

The study of the statistics presented by the essayists this evening indicates that many deaths among premature infants are due to accidents at birth, congenital defects and other causes. In order to determine the exact cause of death, I urge that a postmortem examination be made of all these infants, so that the death certificates may more fully represent the exact pathologic condition.

An effort is being made by the health department of the city to reduce this mortality rate. An educational campaign has been instituted, and prematurity is now "reportable." Ambulance transportation for premature infants born in the home is available by calling the department of health. Premature infants will be transferred to any hospital that the physician may select. The educational campaign of the department of health is based on results obtained in the stations for premature infants of Chicago's larger hospitals. It is hoped that the information so supplied to physicians and hospitals will result in a lower mortality rate for premature infants.

Chicago has the lowest death rate among infants of any large city in the United States; by saving more premature infants we hope to reduce this rate still further.

DR. R. L. JENKINS: I do not believe that the story of hemorrhage is told by any means completely by mortality statistics or by the frank cases of Little's disease. In examining a large number of children in a clinic for child guidance I have been much impressed with the frequency with which one sees children without anything that can be called Little's disease but with minor evidence of injury or disease of the nervous system. There are children who are very excitable, distractible, overactive, "jumpy," more dull than the other members of the family, and on physical examination one obtains on one side an increased knee jerk and a positive Babinski sign or ankle clonus; or perhaps there is a slight athetosis of the hands, which is evident only when the hands are held out straight with the fingers spread. I think that for every case of Little's disease there are half a dozen minor injuries that are passed over. I accept the suggestion that it is difficult to be sure of these things, but because of the frequency in these

cases of an accompanying history of difficult labor I am thoroughly convinced that one has to weigh quite a bit more than the cause of death from cerebral hemorrhage, or frank athetosis or many other things in order to estimate the damage that this accident causes.

DR. ROBERT C. LONERGAN: Being interested in orthopedic surgery, I am considerably interested in Little's disease. Cerebral palsies have been attributed to faulty obstetric procedures, sometimes on the slightest evidence. More is being learned about this condition, yet the neuropathologists do not have any fixed agreement on the etiology of cerebral palsy. The condition cannot be lightly dismissed as Little's disease, for there are all manner of motor injuries. There are the conventional spastic paraplegias which are easily recognized, but there are also conditions, which, as Crothers has pointed out, may be considered as due to extrapyramidal lesions, with disturbances of motion, of speech and of muscular tone of the body. Crothers was among the first to question the etiology in these cases. He also called attention to transection of the cord following injuries received at the time of birth in breech extraction. As Dr. Galloway pointed out, Crothers believes that these are due to traction that is applied over several segments of the cord, producing a fixed lesion, frequently with flaccid paraplegia, although some groups show evidences of spasticity. For these children the prognosis is rather poor. Any one working with crippled children realizes the hopelessness of treatment in many cases of the cerebral palsies. Many patients are found in institutions, and yet with careful study one finds that not all of them have mental defects. Certainly some of them do not have any mental defect, but they do have disturbances of associated movements, as shown in their speech, to a degree that narrows the mental horizon.

I cannot pass over the question of injuries to the brachial plexus without mentioning that the majority of them are rather mild and the treatment is frequently started late. In a definite brachial palsy of the arm, if the arm is elevated and tied to the head of the bed this will frequently suffice. We usually put the arm up in the so-called Statue of Liberty splint, and most of the patients recover. On the North Shore I have never seen complete paralysis of the arm, nor have I seen any paralysis of the Klumpke type. Fracture of the clavicle can be dismissed with a few words, as the treatment is very simple. Usually bandaging the arm with flannel and fastening it to the side is sufficient. I am sure that some cases are overlooked and that the patients get well spontaneously.

DR. CLIFFORD G. GRULEE: I have given a great deal of thought to the question of intracranial hemorrhage of the new-born and wonder whether we are not suffering from tradition and whether we are not taking everything that has been said as a matter of course. In regard to the pathology, what proof have we that many of the conditions that occur later in childhood are due to intracranial hemorrhage rather than to injuries at birth? I have never seen any proof.

As to the diagnosis, I have not been able to diagnose intracranial hemorrhage and am surprised that so many here have said that a certain case was one of intracranial hemorrhage and another was not. I have come to the conclusion that I cannot diagnose this condition and shall give three examples of failure to do so.

Several years ago I went to a hospital to see a child. There were three physicians there when I arrived, and the father of the child was a physician. The child was blue and almost lifeless, and we all agreed that the case was one of intracranial hemorrhage and did not think that the child would live twenty-four hours. The boy is now 15 years old and has gone to school; his father says that except for an inherited dislike of mathematics he has done well.

I saw another case at Wesley Memorial Hospital with Dr. Schacter several years ago. The child was having general convulsions and had one symptom that I had never seen before—unilateral sweating. We decided that the case was one of intracranial hemorrhage. The child eventually died. He did not have intracranial hemorrhage, but a cardiac lesion which we did not diagnose. Another child whom I saw within the last two or three years showed almost the same find-

ings, except that it did not have the sweating. It had the cephalic cry and all the symptoms of intracranial hemorrhage, and yet it had a congenital cardiac lesion which we did not diagnose; it did not have any sign of intracranial hemorrhage at necropsy.

I have come to the conclusion that I can diagnose intracranial hemorrhage only at necropsy. I wonder whether there are not many conditions which are not intracranial hemorrhage that may be traumatic meningitis, as one French author has demonstrated, I think, quite clearly.

DR. A. LEVINSON: I agree with Dr. Grulee that it is very difficult to diagnose cerebral hemorrhage. As a rule, we diagnose it on the necropsy table, but, on the other hand, when a child is restless, has a cephalic cry, moans, has convulsions, is apathetic and has fleeting cyanosis, we may make a diagnosis of cerebral hemorrhage. It was pointed out several years ago that in cases of congenital heart disease the cyanosis is constant, but that in cases of cerebral hemorrhage it is fleeting and becomes worse on exercise. This fact may be utilized in diagnosis.

If a child who presented symptoms of cerebral hemorrhage becomes spastic within a few weeks or months, I think that it is safe to make a diagnosis of cerebral hemorrhage. We do, however, see children who are thought to have cerebral hemorrhage but who suffer from maldevelopment of the brain.

It is hard to diagnose cerebral hemorrhage even on the necropsy table. One of the colored slides that I showed this evening demonstrates how difficult it is to make a differential diagnosis between cerebral hemorrhage and cerebral congestion.

Dr. Abt spoke of the production of cortical changes by meningeal hemorrhage. I think that this occurs in many cases, but, on the other hand, what I wanted to bring out by my lantern slides is that Saphir and I think that it is possible to conceive that a great many minor hemorrhages disappear without producing any scarring at all. If the hemorrhage is intracerebral the patient either dies or may be hopelessly incapacitated. I think, therefore, that there is hope that cerebral hemorrhage does not necessarily produce cortical atrophy in every case.

Encephalography gives information as to the condition of the brain after cerebral hemorrhage. At the Cook County Hospital, we have taken a great many encephalograms in cases diagnosed as those of cerebral hemorrhage and have found that the encephalograms vary. There is the type with an accumulation of air in the subarachnoid space, signifying definite atrophy of the brain; in another type there is so-called arachnoiditis with no air coming through at all; then there are normal encephalograms even in cases of children who are spastic.

A word or two about asphyxia: I believe that in many cases this is a manifestation of cerebral hemorrhage.

Some one mentioned atelectasis. Atelectasis is found in most cases of cerebral hemorrhage. However, we do not consider that every instance of atelectasis is due to cerebral hemorrhage, for it also occurs without this condition.

News and Comment

GENERAL

Physicians Certified by American Board of Pediatrics.—The following have been certified by the American Board of Pediatrics since the last report, on June 6, 1935:

Fred Harold Allen, Holyoke, Mass.; Baird U. Brooks, Durham, N. C.; Charles Edward Conrad, Harrisonburg, Va.; Woodruff L. Crawford, Rockford, Ill.; Brewster Clarke Doust, Syracuse, N. Y.; James Keeley Everhart, Pittsburgh; Horace Lester French, Lansing, Mich.; Leo S. Friedman, Cincinnati; Thurman B. Givan, Brooklyn; Archie Leland Gleason, Great Falls, Mont.; David Greene, New York; Sidney Valentine Haas, New York; Eliot Hubbard Jr., Cambridge, Mass.; Lewis A. Koch, Brooklyn; Lambert Krahulik, Brooklyn; Stanley S. Lamm, Brooklyn; Carl H. Laws, Brooklyn; George Nelson Leonard, Lawrence, N. Y.; Thomas J. McElhenney, Austin, Texas; Henry Allen Reisman, Jamaica, N. Y.; Walker L. Rucks, Memphis, Tenn.; Francis Brooking Schley, Columbus, Ga.; Herbert C. Soule, Rochester, N. Y.; Harold Theodore Vogel, Flushing, N. Y.; Norman Turner Welford, La Grange, Ill.; Charles A. Weymuller, Brooklyn; George Edward White, Windsor, Canada; Frank J. Williams, Albany, N. Y.; King Grier Woodward, Rockford, Ill.; Arthur Fowler Ackerman, Summit, N. J.; Ward L. Chadwick, Grand Rapids, Mich; Sidney Shaw Chipman, Norwalk, Conn.; Nathan H. Einhorn, Philadelphia; Lee Edward Farr, New York; Abe Samuel Finkelstein, Newark, N. J.; Benjamin M. Gasul, Chicago; Fairfax Hall, New Rochelle, N. Y.; Paul Harper, New Haven, Conn.; Marion Gertrude Josephi, New York; Louis Judelsohn, Buffalo; George William Kutscher Jr., Asheville, N. C.; Martin M. Maliner, Brooklyn; John Walker Maroney, Detroit; Laura Elizabeth McClure, Lansdowne, Pa.; Paul Morris, Philadelphia; Wilfred S. Nolting, Detroit; Merle Pierson, Detroit; Alfred Wayland Pinkerton, Dobbs Ferry, N. Y.; Thomas Francis Reilly, Springfield, Mass.; Robert Page Rogers, Greenwich, Conn.; Harold B. Rothbart, Ann Arbor, Mich.; Jacob Lewis Rothstein, New York; Russell B. Scobie, New York; John J. Slavens, Toronto, Canada; Lendon Snedeker, Boston; Elwood Wakefield Stitzel, Altoona, Pa.; Haskell Talamo, Worcester, Mass.; Harry Wexler, Brooklyn; Edward Theodore Wilkes, New York; Herbert M. Williams, New York.

In this group thirty-one took the examination. At that examination, which was held in Atlantic City, N. J., on June 10 and 11, forty-six men took the examination and fifteen failed. Of the group that failed, seven were in Group I, one in Group II and seven in Group III. Of the group that passed, two were in Group I, seven in Group II and twenty-two in Group III.

T. Wood Clarke, Utica, N. Y.; Harry R. Litchfield, Brooklyn; Arthur C. Swartz, Albany, N. Y.; Horace Kent Tenney Jr., Madison, Wis.

None of these was examined.

SOCIETY NEWS

International Association for Preventive Pediatrics.—The Fifth Conference of the International Association of Preventive Pediatrics (Medical Section of the Save the Children International Union) will be held at Basel, Switzerland, under the chairmanship of Professor Wieland, Friday and Saturday, Sept. 20 and 21, 1935.

The subjects to be discussed and the names of the reporters are:

1. Measures Proper for the Avoidance of Inside and Outside Contamination in Children's Hospitals and Rules to Be Observed to This End (*a*) in the Construction of Such Hospitals and (*b*) in Their Management. Dr. M. Lust, Brussels; Professor Fanconi, Zurich, and Professor Husler, Munich.

2. Prevention of Tuberculosis in Schools (the subject will be strictly limited to school age). Dr. J. H. Tuntler, Groningen; Dr. Génévrier, Paris, and Professor Kleinschmidt, Cologne.

Those who desire to be present at the conference, as well as to take part in the discussions following the reports, are requested to communicate with the secretary of the association, 15 rue Lévrier, Geneva, Switzerland.

Book Reviews

Tuberculosis: A Book for the Patient. By Fred G. Holmes. Price, $2. Pp. 312. New York: D. Appleton-Century Co., Inc., 1935.

This nontechnical volume, dealing not only with various phases of tuberculosis and its treatment but also with the relationship of the patient to the physician, makes no pretense of presenting information of interest to the medical profession.

Holmes presents the subject in a conservative manner, but he unfortunately minimizes the importance of applying tuberculin tests to adults. The chapter devoted to the choice of physicians may tend, in certain instances, to disturb the patient's confidence in the family physician.

The advisability of discussing the disadvantages and complications of different types of collapse therapy, as has been done in this volume intended for the laity, is debatable. These questions might preferably be left to the physician, who, on the basis of his knowledge and judgment, is in a position not only to explain the indicated method of treatment in detail and to answer questions not adequately covered by a book, but also to prevent the development of unjustified prejudices in the mind of the partially informed and easily mistaken patient against valuable but technical therapeutic procedures.

It is suggested that physicians familiarize themselves with the contents of this volume if they contemplate recommending it to their patients.

Bee Venom Therapy. By Bodog F. Beck. Price, $5. Pp. 238. New York: D. Appleton-Century Company, Inc., 1935.

For hundreds of years the sting of bees has been credited with unusual theraputic success in rheumatic conditions. Beck has made a careful study of bee venom therapy, has used it extensively, and has tried to be impartial and scientific in the evaluation of the results. His enthusiasm and confidence in the beneficial effects of bee venom in rheumatic states permeates this very interesting book. He anticipates a skeptical and distrustful attitude from the medical profession, but is thoroughly convinced of the real merit and extraordinary efficacy of this agent.

The medical history of the bee and its venom is an absorbing story. The chemistry and physiologic effects of the venom are discussed as fully as present knowledge permits. Literally hundreds of reports of the use of bee venom have been collected from many countries. The method of collecting the venom, the indications for its use and the details of the treatment are fully described. The results of a questionnaire sent to hundreds of bee-keepers is presented. It is the author's aim to produce a textbook on bee venom therapy and to stimulate professional interest and research in apitherapy.

Growth and Development of the Young Child. By Winifred Rand, Mary E. Sweeny and E. Lee Vincent. Price, $2.75. Pp. 429, with 57 illustrations. Philadelphia: W. B. Saunders Company, 1934.

In this book the authors have collected the latest knowledge concerning the physical and mental growth of infants and young children. It is written for the laity and is designed for use as a text in a study group. At the end of each chapter is a list of questions for use in discussion. The material for this textbook was obtained from the best of recent publications, and the bibliography at the end of each section suggests references for use in collateral reading.

The psychology of the small child and his relation to the family are thoroughly discussed. The prenatal care of the mother is also considered. One chapter is devoted to the care and feeding of the baby.

This book is highly recommended as a text for a group of mothers who desire to obtain a better understanding of the behavior, growth and physiologic processes of young children. The authors are associated with the Merrill-Palmer School for the teaching of child care and training, located in Detroit.

Tuberculosis of the Lymphatic System. By Richard H. Miller, M.D., F.A.C.S. Price, $4. Pp. 248, with 18 illustrations. New York: The MacMillan Company, 1934.

This is a complete clinical presentation of tuberculosis of the lymphatic system, especially as it is encountered in a large clinic for patients with extrapulmonary tuberculosis. The historical summary is of great interest. The anatomic and clinical considerations of disease of the lymph nodes in various parts of the body are well presented. The discussion of the etiology and pathogenesis embraces modern theories, as exemplified in an extensive bibliography. Perhaps it is not to be expected that a surgeon would find time to acquaint himself with all the important literature, and in some respects the portions of the book devoted to pathogenesis are somewhat didactic and superficial. Also, the agency of the bovine bacillus in the causation of tuberculosis in the United States possibly is unduly emphasized. Certainly this applies to the child in the city, as contrasted with the child in the country. On the whole, the book cannot fail to be of interest to any one who is especially concerned with tuberculosis of the lymphatic system.

Diseases of the Skin. By S. Ernest Dore and John L. Franklin. Price, $5. Pp. 387, with 46 illustrations. New York: D. Appleton-Century Company, Inc., 1934.

This small book on diseases of the skin was written by two English dermatologists as a handbook for practitioners and students. The original intention was to revise the well known textbook "Diseases of the Skin" by the late Sir Malcolm Morris. As the revision progressed it became evident that so much new material had to be introduced that the book had become virtually a new one.

Dore and Franklin have adhered to their purpose of making the book concise and yet sufficiently comprehensive to meet the needs of physicians other than specialists in the field of dermatology.

The first chapter deals with the anatomy, physiology and pathology of the skin. In the second chapter the principles of diagnosis are discussed. The remainder of the book is devoted to the diagnosis and treatment of diseases of the skin, with strict avoidance of lengthy discussions and unnecessary words. The work is admirably constructed as a textbook for the student or as a ready reference book for the general practitioner.

Die banale Grippe des Kindes. Beihefte zum Archiv fur Kinderheilkunde, No. 5. By Prof. Dr. Erich Müller. Price, 2 marks. Pp. 31. Stuttgart: Ferdinand Enke, 1934.

This entire monograph is devoted to a clinical discussion of common grip as it occurs in children. Müller considers grip to be a generalized infection due to an ultramicroscopic virus. The complications, however, are attributed to secondary invasion by bacteria which are normally present in the body but become pathogenic because of the conditions produced by the disease. There is a lengthy discussion of the complications and sequelae, i. e., cervical adenitis, otitis media, sinusitis of the nasal accessory cells, bronchitis, pneumonia, enteritis, urinary infections, cardiovascular disturbances, cerebral manifestations, rheumatic symptoms and purpura. In the prophylaxis of grip the avoidance of contact with ill children is advised, but most important of all is the building up of the nutrition and resistance of the child by proper diet, sunshine, rest, exercise and other factors. The general management of the patient with grip and the special treatment of each of the complications are discussed in detail.

Directory of Pediatric Societies *

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor G. Scheltema, 6a Heereplein, Groningen, The Netherlands.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.
Place: Bâle, Switzerland. Time: September 1935.

FOREIGN

British Paediatric Association

President: Dr. Hugh Thursfield, 84, Wimpole St., London, W. 1.
Secretary: Dr. Arthur G. Maitland Jones, 31 A, Weymouth St., London, W. 1.

Royal Society of Medicine, Section for the Study of Disease in Children

President: Dr. R. C. Jewesbury, 5, Wimpole St., London, W. 1.
Secretary: Dr. Helen Mackay, 28, John St., London, W. C. 1.
Place: 1, Wimpole St., London. Time: Fourth Friday of each month, 4:30 p. m.

Paediatrický Spolok na Slovensku

President: Dr. A. J. Chura, Lazaretská 6, Bratislava, Czechoslovakia.
Secretary: Dr. S. Limbacher, Dlhá 2, Bratislava, Czechoslovakia.
Place: Pediatric Clinic, University, Bratislava. Time: Six times a year.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. Horton R. Casparis, Vanderbilt University Hospital, Nashville, Tenn.
Secretary: Dr. Ralph M. Tyson, 255 S. 17th St., Philadelphia.
Place: Kansas City, Mo. Time: 1936.

American Academy of Pediatrics

President: Dr. Thomas B. Cooley, 1728 Seminole Ave., Detroit.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.
Region I. Place: Philadelphia. Time: Oct. 11-12, 1935.
Regions II and III. Place: St. Louis. Time: Nov. 8-9, 1935.
Region IV. Place: Seattle, with North Pacific Pediatric Society. Time: Aug. 9-10, 1935.

American Child Health Association

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. Philip Van Ingen, 125 E. 71st St., New York.

American Hospital Association, Children's Hospital Section

President: Mr. Robert Witham, Children's Hospital, Denver.
Secretary: Miss Agnes O'Roke, Kosair Crippled Children's Hospital, Louisville, Ky.
Place: St. Louis. Time: Sept. 30-Oct. 4, 1935.

American Pediatric Society

President: Dr. Fritz B. Talbot, 270 Commonwealth Ave., Boston.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid St., St. Louis.

Canadian Society for the Study of Diseases of Children

President: Dr. D. P. Arnold, 159 Bidwell Parkway, Buffalo, N. Y.
Secretary-Treasurer: Dr. R. R. Struthers, 1414 Drummond St., Montreal.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

SOCIETY FOR PEDIATRIC RESEARCH

President: Dr. C. F. McKahnn, Children's Hospital, Boston.
Secretary: Dr. A. A. Weech, 3975 Broadway, New York.

SECTIONAL

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. Armin Rembe, Stimson Bldg., Seattle.
Secretary: Dr. Frank H. Douglass, 1227 Medical and Dental Bldg., Seattle.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON PEDIATRICS

Chairman: Dr. Oliver W. Hill, 301 Medical Arts Bldg., Knoxville, Tenn.
Secretary: Dr. Madison Hines Roberts, 104 Ponce de Leon Ave., N. E., Atlanta, Ga.

STATE

ALABAMA PEDIATRIC SOCIETY

President: Dr. J. W. Britton, 931 Noble St., Anniston.
Secretary-Treasurer: Dr. Wallace Clyde, Employees' Hospital, Fairfield.

ARKANSAS STATE PEDIATRIC ASSOCIATION

Chairman: Dr. Morgan Smith, 625 Beech St., Little Rock.
Secretary: Dr. Madeline A. M. Melson, 2111 N. Spruce St., Little Rock.

GEORGIA PEDIATRIC SOCIETY

President: Dr. William Willis Anderson, 478 Peachtree St., Atlanta.
Secretary-Treasurer: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Place: Atlanta, December 1935. Savannah, June 1936.

INDIANA STATE PEDIATRIC SOCIETY

President: Dr. Louis H. Segar, 23 E. Ohio St., Indianapolis.
Secretary-Treasurer: Dr. Mathew Winters, 23 E. Ohio St., Indianapolis.
Time: Two meetings a year.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. Charles James Bloom, 3439 Prytania St., New Orleans.
Secretary-Treasurer: Dr. J. A. Crawford, 834 Ryan St., Lake Charles.

MEDICAL SOCIETY OF STATE OF NEW YORK, SECTION ON PEDIATRICS

Chairman: Dr. George M. Retan, 459 James St., Syracuse.
Secretary: Dr. John D. Craig, 33 E. 61st St., New York.
Place: New York City. Time: April 27-29, 1936.

MICHIGAN STATE MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Secretary: Dr. C. R. Dengler, 131 W. Michigan Ave., Jackson.
Place: Flint. Time: September 1935.

MISSISSIPPI STATE PEDIATRIC SOCIETY

President: Dr. R. E. Wilson, 205 S. Harvey St., Greenville.
Secretary-Treasurer: Dr. Guy C. Jarratt, 920 Crawford St., Vicksburg.
Place: To be designated by Society. Time: Yearly.

NEBRASKA PEDIATRIC SOCIETY

President: Dr. J. A. Henske, 1614 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. J. H. Murphy, 915 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. J. R. Ashe, 306 N. Tryon St., Charlotte.
Secretary: Dr. R. A. Moore, 306 N. Tryon St., Charlotte.
Place: Various children's hospitals. Time: Twice a year.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. Julian Feild, 610 S. Monroe St., Enid.
Secretary: Dr. B. H. Nicholson, 301 N. W. Twelfth St., Oklahoma City.

PENNSYLVANIA MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Francis T. O'Donnell, 345 North Main St., Wilkes-Barre.
Secretary: Dr. Theodore O. Elterich, 119 S. Highland Ave., Pittsburgh.
Place: Harrisburg. Time: Sept. 30-Oct. 3, 1935.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. William Weston Jr., 1428 Lady St., Columbia.
Secretary-Treasurer: Dr. Leland B. Salters, 317 S. Warley Ave., Florence.

TENNESSEE STATE PEDIATRIC SOCIETY

President: Dr. Joe T. Smith, 702 Medical Arts Bldg., Knoxville.
Secretary: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.
Place: Memphis. Time: April 1936.

TEXAS PEDIATRIC SOCIETY

President: Dr. C. O. Terrell, 813 Medical Arts Bldg., Fort Worth.
Secretary-Treasurer: Dr. F. H. Lancaster, 1507 Medical Arts Bldg., Houston.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. W. P. McDowell, 142 W. York St., Norfolk.
Secretary: Dr. W. A. McGee, 616 W. Grace St., Richmond.

WEST VIRGINIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

President: Dr. John T. Thornton, 58, 16th St., Wheeling.
Secretary: Dr. Claude L. Holland, 400 Locust Ave., Fairmont.

LOCAL

ACADEMY OF MEDICINE OF BROOKLYN, PEDIATRIC SECTION

President: Dr. Harry M. Greenwald, 499 Ocean Ave., Brooklyn.
Secretary: Dr. Sylvan D. Lazarus, 847 Lincoln Place, Brooklyn.
Place: Medical Society of County of Kings Bldg., 1313 Bedford Ave., Brooklyn.
Time: Third Wednesday of each month from October to May, 8:30 p. m.

ACADEMY OF MEDICINE OF CLEVELAND, PEDIATRIC SECTION

Chairman: Dr. J. A. Garvin, Carnegie Medical Bldg., Cleveland.
Secretary: Dr. William M. Champion, 2323 Prospect Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

ACADEMY OF MEDICINE, TORONTO, SECTION OF PEDIATRICS

President: Dr. C. V. Mulligan, 17 Walmer Rd., N., Toronto.
Secretary: Dr. T. B. Verner, 170 St. George St., Toronto.

BRONX PEDIATRIC SOCIETY

President: Dr. Harry M. Shapiro, 1882 Grand Concourse, New York.
Secretary: Dr. Daniel J. Dolan, 420 E. 159th St., New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

BROOKLYN ACADEMY OF PEDIATRICS

President: Dr. W. F. Watton, 240 Berkeley Pl., Brooklyn.
Secretary: John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Thursday of April and September.

CHICAGO PEDIATRIC SOCIETY

President: Dr. A. Levinson, 30 N. Michigan Ave., Chicago.
Secretary: Dr. James H. Wallace, 715 Lake St., Oak Park, Ill.
Place: College Hall, John B. Murphy Hospital. Time: Third Tuesday of each month.

DALLAS COUNTY PEDIATRIC SOCIETY

President: Dr. P. E. Luecke, 4105 Live Oak St., Dallas, Texas.
Secretary: Dr. R. S. Usry, 1835 Garrett Ave., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., first and third Saturdays of each month.

DETROIT PEDIATRIC SOCIETY

President: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Secretary: Dr. W. J. Scott, 5140 Second Ave., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month.

FULTON COUNTY MEDICAL SOCIETY, PEDIATRIC SECTION (ATLANTA, GA.)

Chairman: Dr. Joseph Yampolsky, 478 Peachtree St., Atlanta.
Secretary: Dr. T. I. Willingham, 384 Peachtree St., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

HARRIS COUNTY PEDIATRIC SOCIETY

President: Dr. Byron P. York, 3820 Fannin St., Houston, Texas.
Secretary-Treasurer: Dr. E. O. Fitch, 3717 Main St., Houston, Texas.
Place: Houston Club. Time: Third Monday of each month.

INTERMOUNTAIN PEDIATRIC SOCIETY

President: Dr. Helmina Jeidell, 11 Exchange Pl., Salt Lake City, Utah.
Secretary-Treasurer: Dr. Edwin R. Murphy, 9 Exchange Pl., Salt Lake City, Utah.
Place: Salt Lake City, General Hospital. Time: First Thursday of each month, 8 p. m.

KANSAS CITY (MISSOURI) PEDIATRIC SOCIETY

President: Dr. Harry M. Gilkey, 1103 Grand Ave., Kansas City.
Secretary: Dr. S. A. Stadler, 6133 Brookside Blvd., Kansas City.
Place: Kansas City General Hospital. Time: On call.

MEDICAL SOCIETY OF THE COUNTY OF QUEENS, INC., SECTION ON PEDIATRICS

Chairman: Dr. Henry A. Reisman, 148, 88th Ave., Jamaica, L. I.
Secretary-Treasurer: Dr. Edith A. Mittell, 112 Queens Blvd., Forest Hills, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. W. D. Mims, 1042 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. W. R. Graves, 1193 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month, except June, July and August, 8 p. m.

MILWAUKEE PEDIATRIC SOCIETY

President: Dr. J. Gurney Taylor, 324 E. Wisconsin St., Milwaukee.
Secretary: Dr. H. B. Miner, 425 E. Wisconsin Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. Paul Emerson, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. Henry E. Gallup, 66 Commonwealth Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

Chairman: Dr. Béla Schick, 17 E. 84th St., New York.
Secretary: Dr. Alexander T. Martin, 107 E. 85th St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. E. F. Robb, 1801 Lyndale Ave., S., Minneapolis.
Secretary: Dr. A. V. Stoesser, University Hospital, Minneapolis.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala, Pa.
Secretary: Dr. James E. Bowman, 4091 Comly St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

PITTSBURGH PEDIATRIC SOCIETY

President: Dr. Carl K. Wagener, Jenkins Arcade, Pittsburgh.
Secretary-Treasurer: Dr. E. R. McClusky, 3200 Fifth Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Tuesday, alternate months from October to April, inclusive.

RICHMOND PEDIATRIC SOCIETY

President: Dr. W. A. McGee, 616 W. Grace St., Richmond, Va.
Secretary-Treasurer: Dr. Emily Gardner, 1100 W. Franklin St., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month (except July, August and September).

ROCHESTER PEDIATRIC SOCIETY

President: Dr. H. F. Rowley, 176 S. Goodman St., Rochester, N. Y.
Secretary: Dr. J. M. Parker, 26 S. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month.

ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. Ralph Verploeg, 1850 Gilpin St., Denver.
Secretary: Dr. Max M. Ginsburg, Metropolitan Bldg., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 2:30 p. m.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. J. V. Cooke, St. Louis Children's Hospital, St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, Beaumont Bldg., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

SEATTLE PEDIATRIC SOCIETY

President: Dr. Arthur E. Wade, 1215, 4th Ave., Seattle.
Secretary: Dr. Walter B. Seelye, Cobb Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Victor E. Stork, 1136 W. Sixth St., Los Angeles.
Secretary: Dr. Howard R. Cooder, 3875 Wilshire Blvd., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

UNIVERSITY OF MICHIGAN PEDIATRIC AND INFECTIOUS DISEASE SOCIETY

President: Dr. Daniel Budson, 3001 W. Grand Blvd., Detroit.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.
Place: Ann Arbor, Mich. Time: Nov. 22-23, 1935.

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